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CONTENTS

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THE NECROBIOTIC NODULES OF RHEUMATOID ARTHRITIS

CASE IN WHICH THE SCALP, ABDOMINAL WALL (INVOLVING STRIPED MUSCLE), LARYNX, PERICARDIUM (INVOLVING MYOCARDIUM), PLEURAE (INVOLVING LUNGS), AND PERITONEUM WERE AFFECTED

BY

RONALD W. RAVEN, F. PARKES WEBER, and L. WOODHOUSE PRICE

Much has been written about the nodules of rheumatoid arthritis, which, though present in less than a quarter of the patients, may nevertheless be regarded as constituting an important, if not the most important, feature from the pathological point of view. Collins (1937) and others, including Parkes Weber (1943, 1944), Kersley and others (1946) have shown that the characteristic subcutaneous nodules consist of foci of fibrinoid degeneration and necrosis, surrounded by a border of tissue reaction, notably by a palisade-like radiate arrangement of fibroblasts. Somewhat similar microscopic appearances have been described in pathological conditions of a different nature (granuloma annulare, necrobiosis lipoidica), but even if the histological features of the nodules of rheumatoid arthritis were absolutely pathognomonic, one would still be far from the discovery of the essential pathogenic agent.

Allison and Ghormley (1931) made a great point of what they called "focal collections of lymphocytes" in the synovial membrane of joints being almost pathognomonic of "proliferative arthritis of uncertain origin"—that is to say, of rheumatoid arthritis. But if one looks at their illustrations (for instance, p. 147, fig. 4; p. 169, fig. 3; and Plate VIII) one recognizes the presence (in these "focal collections") of so-called "germ-centres" of Flemming. Now, surely such lymphadenoid foci with typical "germ-centres" can hardly be considered as pathognomonic of any special disease. Apart from their conspicuous presence in normal lymphadenoid tissue (lymph glands, tonsils, the walls of the vermiform appendix and intestines, the Malpighian corpuscles of the spleen), they form a special feature in so-called lymphadenoid goitres, and are also not rarely found in thyroids from patients with Graves' disease. One of us (Parkes Weber) has seen them in abnormal salivary glands. They constitute a conspicuous feature of cutaneous lymphocytomata (Epstein, 1935), and may be found in various other pathological conditions (Parkes Weber, 1947).

Similarly, there is nothing absolutely pathognomonic in the painless lymphadenopathy of the superficial lymph-glands, which is present during active periods in many cases of rheumatoid arthritis, though seldom noticed by the patients themselves and often not looked for by the examining doctor. It is "non-specific follicular lymphadenopathy" of toxic or infective origin, with marked enlargement of the "germ-centres" of Flemming (not to be confused with "follicular lymphoblastoma" of neoplastic nature), and tends to disappear when the patient's general and articular condition improves and the disease becomes quiescent (Parkes Weber, 1947, p. 38, case 4). Rochu (1946) thinks that this lymphadenopathy, together with the articular changes and occasional splenomegaly, indicates that what we in England call rheumatoid arthritis—which cannot be separated from the Chauffard-Still-Felty syndrome—is much more than a joint disease and that the reticulo-endothelial system is obviously involved.

As to possible pathogenic relationship between rheumatoid arthritis and rheumatic fever and between their respective nodules (cf. Bennett and others, 1940), there has been much discussion. Most of those who have studied the question apparently have come to the conclusion that the two diseases are clinically distinct and probably not due to the same (still unknown) pathogenic agent. Dawson (1933), however, in his "Comparative study of Subcutaneous Nodules in Rheumatic Fever and Rheumatoid Arthritis" wrote: "These studies . . . lend further support to the conception that

rheumatic fever and rheumatoid arthritis are intimately related and possibly different responses of affected individuals to the same aetiological agent."

In rheumatic fever the nodules mostly remain small and soon disappear. Small nodules in rheumatoid arthritis also sometimes disappear rapidly, but most of the nodules, especially the larger ones, become chronic and are only slowly, if at all, absorbed—doubtless owing to the formation of the characteristic necrotic foci surrounded by chronic reactive inflammatory and firm fibrous tissue. Fresh nodules may appear—a sign of renewed activity—even in old quiescent and apparently "burnt-out" cases.

Case Report

History.—The patient, a woman, aged 62, was admitted to the Royal Cancer Hospital under one of us (R. W. Raven) on March 14, 1947, on account of increasing difficulty in breathing. This commenced about January, 1946, and steadily progressed with increasing inspiratory stridor. Eventually the patient was suffering from breathlessness whilst at rest.

In April, 1946, there was onset of dysphagia, with special difficulty in the swallowing of fluids, which were often regurgitated. There was also progressive loss of voice, which became more and more indistinct and of a croaking character.

In December, 1946, the patient noticed the appearance of multiple lumps on her head. Whilst under observation similar lumps developed over the abdomen. There were also nodules on the elbow-joints and hands, some of which probably dated from the commencement of rheumatoid arthritis in 1916.

From October, 1946, there was increasing difficulty in vision, associated with gross conjunctivitis, which later progressed until, by the middle of March, 1947, she could only vaguely appreciate any object. There was marked loss of weight and energy, and the appetite was poor. No symptoms related to the colon or gastro-intestinal tract were noted.

The patient had no children, but had had five miscarriages. She had had rheumatic fever in 1905, and in 1916 showed the onset of progressive chronic rheumatoid arthritis.

Condition on Examination.—Arthritic changes involved the joints of the arms and legs, with gross deformity. The patient was noticed to breathe with a marked inspiratory stridor, with all the accessory respiratory muscles in action. There was obvious great loss of weight.

Numerous nodules were present in the subcutaneous tissues of the scalp, some of which were attached to the skin and some attached deeply to the epicranial aponeurosis. The nodules were most marked on the forehead, but were scattered throughout the scalp. They varied in size from 1 cm. to 3 cm. in diameter.

The conjunctivae were pale, and there was an extensive ulcerative scleritis with corneal involvement which, in the left eye especially, had the clinical appearance of a Mooren's ulcer.

There were numerous hard nodules about the elbow joints, attached to the skin, and on the left side ulcerated.*

The subcutaneous tissue of the abdomen showed multiple scattered nodules, whereas none was seen over the chest.

There was a painless lymphadenopathy of the superficial lymph-glands, such as is often present during the active stages of rheumatoid arthritis (see above).

There was a patch of dry gangrene on the tip of the right great toe, and no pulsation could be felt in either arteria dorsalis pedis.

Radiographic Investigations.—Radiographs of the chest showed bronchitic changes in the lungs and some cardiac enlargement. No abnormality detected on radiographic examination of the skull.

There were advanced changes of rheumatoid arthritis in all the joints, with marked osteoporosis and skeletal deformity. A radiograph of the larynx showed a projection from the posterior wall at the level of the epiglottis.

Haematology.—There were 4,660,000 red blood cells and 8,000 white blood cells per c.mm. The Hb was 75 per cent.; Wassermann and Kahn reactions were negative. The erythrocyte sedimentation rate was 40 mm. in one hour (Westergren).

Blood urea, blood uric acid, serum calcium, serum inorganic phosphorus, and serum phosphatase were all within normal limits. There was nothing abnormal in the urine.

Progress.—The patient developed signs of pneumonia. Her condition deteriorated, and she died on March 30, 1947.

This patient had been seen by one of us (F. Parkes Weber), who agreed that the case was one of advanced chronic nodular necrobiosis of the rheumatoid arthritis type. The biopsy tissue (see below) had been found superficially to resemble that of a gumma.

Post-mortem Report

External Examination.—The body was that of a poorly developed, poorly nourished, and extremely deformed woman of about 60 years of age. A small surgical incision was seen on the anterior aspect of the right temple. In the left temporal region were three or four small, firm, circumscribed subcutaneous nodules. They did not fluctuate, and were not attached to the overlying skin. A number of smaller nodules were seen and felt beneath the skin round the elbow and wrist joints and in the anterior abdominal wall. The degree of joint deformity was considerable, and the wrists and hands displayed an exaggerated ulnar deviation with wasting of the interosseous muscles, presenting a picture of advanced rheumatoid arthritis. In the legs it was hardly possible to move the ankle joints, and the left tibia showed an almost complete backward dislocation.

Internal Examination.—The scalp showed no abnormality, apart from that already mentioned, and the skull appeared to be of normal thickness. The brain was

* One of us (F. Parkes Weber) has since heard of two (unpublished) cases with ulcerated nodules of the rheumatoid arthritis type.

normal in appearance. There was no meningitis or flattening of the cerebral convolutions. The ventricles contained a normal amount of cerebrospinal fluid, and the arteries at the base of the brain did not present any gross evidence of atheroma.

The mouth was edentulous and the tongue, larynx, pharynx, thyroid, and trachea presented no obvious macroscopic evidence of pathological change, excepting a few small submucous nodular thickenings in the region of the glottis, particularly one on the epiglottis.

The left lung was adherent at its apex. It was partly collapsed by a left basal effusion and the visceral pleura was covered by a fairly thick fibrinous exudate. The cut surface of this lung showed the characteristic appearance of collapse, and there was some evidence of bronchitis. Pulmonary emboli were not found.

The right lung was also adherent to the parietal pleura and a small amount of turbid fluid was found at its base. This lung also was covered by fibrinous exudate which had involved the mediastinum and pericardium; on the left side the diaphragm and the splenic capsule were involved, producing an obvious perisplenitis.

The pericardium was adherent over the anterior surface of the heart; and, on forcible removal, both visceral and (to a less extent) parietal pericardia were found to be studded with raised, whitish firm nodules of 1 to 10 mm. in diameter. There was apparently no calcification. The heart was normal in size and it showed some dilatation of the left auricle with a moderate degree of mitral stenosis. On the endocardial surface of the left auricle there were some nodules of a similar nature to those found on the pericardium, although the process in this instance appeared to be of a minor degree. Further dissection of the heart was not done, with a view to preserving it as a museum specimen, but what could be seen of the aorta and aortic valve did not show any obvious evidence of syphilitic aortitis. The heart muscle, in so far as it was examined, did not appear macroscopically grossly abnormal.

The diaphragm was thickened by a fibrinous exudate which, although penetrating on the left side to involve the spleen, had not produced on the right side any noticeable peri-hepatitis.

The liver was normal in size. Its cut surface did not present any abnormal features and the gall-bladder contained about 3 c.cm. of bile. Gall-stones were not found. The bile-ducts were patent. The gastro-intestinal tract appeared normal throughout. The adrenals were normal.

The kidneys were normal in size and the renal pelves showed no evidence of pyelitis; the capsules were easily stripped off, showing some degree of granulation of the kidney cortex. The ureters and urinary bladder appeared normal.

The uterus and ovaries, together with their ligaments, did not show any abnormal features.

Cause of Death.—The cardiac condition was thought to have been the cause of death.

Summary of Naked-Eye Pathological Findings.—Naked-eye pathological examination showed pericarditis, endocarditis, and mediastinitis; bilateral pleural effusion; perisplenitis; and rheumatoid arthritis.

Histological Examination

Lung and Pleura.—The latter showed fibrous thickening, in which there were several areas of necrosis of varying size from about 0·1 mm. up to 5 mm. These showed some peripheral palisading of nuclei, but in general the appearances were not so characteristic as in the nodules in the heart muscle. Giant cells were inconspicuous.

In sections stained with Orcein much fragmentation of elastic fibres by the necrotic process was discernible.

Rectus Abdominis Muscle.—This showed very clearly demarcated necrobiotic nodules. Muscle bundles were separated, and in several instances the sarcolemma sheath was either destroyed or invaded by proliferating cells.

Heart Muscle.—Sections stained with Van Gieson showed interstitial fibrosis of the muscle fibres, partly in association with necrobiotic nodules, but more frequently remote from the immediate vicinity of such nodules. In addition there was some deposition of calcium salts. The nodules in the heart muscle were sharply demarcated and of characteristic appearance, the peripheral zone of radiating fibroblasts being particularly clear.

A careful search of the heart muscle remote from the necrobiotic nodules failed to reveal any characteristic Aschoff's nodes in the perivascular zones.

Spleen.—The splenic pulp was markedly congested, and the arterioles showed well-marked hyaline degeneration of their medial coats. Some perivascular fibrosis was present, and slight atheromatous changes were seen. A notable feature was the presence of multiple confluent areas of necrobiosis in the thickened capsule. These presented the characteristic morphology of the necrobiotic nodules of rheumatoid arthritis, though giant cells were inconspicuous. The Malpighian bodies were prominent.

Liver.—Brown atrophy was present, and there was a mild degree of cloudy swelling. Certain areas showed congestion, but there was no gross pathological change. No fibrosis was discernible other than a mild degree in certain portal areas.

Kidney.—The cortex showed patches of fibrosis and lymphocytic infiltration associated with glomerular sclerosis and arteriolar sclerosis. The renal tubules showed well-marked stellate lumina produced by cloudy swelling.

Brain and Pituitary.—These showed no gross pathological change.

Larynx: Epiglottic Nodule.—The sagittal section in the midline was passed through the epiglottis and base of the tongue.

Microscopic examination showed multiple foci of necrobiosis in the sub-epithelial zones of the epiglottis, and also in the musculature of the tongue. These foci presented the characteristic histological picture as described in the note on the general histology of these nodules (see further on). Several areas showed hyaline degeneration. Nuclear hyperchromia and pyknosis were well marked. Nuclear palisading was present, and giant cells of the Touton type were frequent. The characteristic lesions were well marked among mucin-secreting accessory salivary glands. The involved tongue

musculature showed interstitial fibrosis, atrophy, and hyaline change.

Nodule from the Forehead.—A nodule from the forehead (biopsy) showed necrobiotic foci surrounded by reactive cellular areas, containing multi-nuclear giant cells (some of Touton type).

Histology of the Nodules.—Characteristically the change was multifocal. Typical lesions from the heart muscle showed numerous minute foci of necrosis. These were approximately $0{\cdot}5 \times 1$ mm. in diameter. The central zone showed pyknosis, karyorrhexis, karyolysis, and a fine powdery deposition of calcium salts.

External to this there was a narrow zone where all structure was lost and which remained almost unstained by eosin. Immediately external to this structureless zone there was some cellular concentration which tended to show palisading of the nuclei and which gave the general effect of cells radiating centrifugally from the central necrotic area. The cells concerned comprised lymphocytes, plasma cells, histiocytes, and small multinucleated giant cells. Some of the latter were of Touton form with a more or less complete peripheral ring of hyperchromic nuclei; others bore a slight resemblance to the tuberculous giant cell.

These centres of necrobiosis were in some cases isolated and occurred in small groups, each separated from its neighbour by normal adipose or muscular tissue. In other instances the necrotic foci became confluent, giving rise to elongated and tortuous masses which presented the characteristic histological features from within outwards, as above described.

We are greatly indebted to Professor D. S. Russell for the following report.

"The specimens received had been fixed in formaldehyde and consisted of (1) a portion of heart muscle, with pericardium, measuring $2{\cdot}8 \times 1{\cdot}1 \times 1$ cm. The pericardium was expanded by two opaque greyish-white firm nodules, the larger of which measured 0·7 cm. The muscle showed no naked-eye changes. (2) A portion of skin and subcutaneous tissues, from the elbow, measuring $3{\cdot}2 \times 1{\cdot}4 \times 1$ cm. Beneath the skin lay a nodular mass, 1·4 cm. in diameter, of firm opaque greyish-white tissue of tough, somewhat fibrous consistency.

One half of each specimen was embedded in paraffin wax; frozen sections were prepared from the remainder and were stained with Sudan III. Unstained frozen sections were mounted for examination with polarized light.

Microscopic Examination

(1) *Heart.*—The visceral pericardium is everywhere thickened by a slight increase of collagenous fibres, sparse infiltration with small lymphocytes and plasma cells, and an increase in small blood vessels which are engorged. There is great focal expansion of this layer by three nodules. The largest shows a large central acellular area of serpiginous outline; much of it appears fibrinoid, but in places, especially towards the periphery, there are many delicate collagenous fibres, and in places ill-defined granular areas packed with fragmented leucocytes. This acellular central area is surrounded by a dense zone of short spindle, and angular, polymorphic cells with round, oval, rod, or occasionally lobed, nuclei and abundant basophil cytoplasm. These cells are often arranged as a palisade, their long axes radiating towards the central area. Small multinucleated giant cells are occasionally present. There are no foam cells. The cells are supported by delicate collagen fibres, which in places coalesce to form small hyaline foci. At the periphery of the nodule is an indefinite zone of infiltration with small round cells blending with that in the remainder of the pericardium.

Frozen sections stained for fat show sparse, fine extra-cellular granules throughout the central necrotic area. Intra-cellular droplets of larger size are numerous within the cells immediately surrounding the necrosis, thereby rendering the zone conspicuous under low powers of the microscope. None is to be found in the periphery of the nodule.

With polarized light some of the intracellular Sudanophil material appears doubly refractive, but the central extra-cellular granules are isotropic.

The myocardium shows, in the interstitial tissue at the extreme edge of the block, a nodule resembling the largest focus in the pericardium. It is almost completely surrounded by bundles of muscle fibres, but, from the curvature of the section, it must lie close beneath the pericardium. The muscle is normal, apart from granules of lipofuscin at the poles of the fibre nuclei.

(2) *The subcutaneous lesion* from the elbow expands the dermis and is composed of aggregated nodules of varying size separated by narrow strands of connective tissue. The largest nodules, measuring up to 8 mm., are central and are composed almost entirely of hyaline collagenous tissue. Many areas are devoid of cells; elsewhere sparse fibroblasts separate the fibres. Near the centres of these larger nodules there are, however, a few ill-defined acellular fibrinoid foci occasionally containing angular spaces. The margins of these foci contain delicate collagenous fibres.

Eight smaller nodules, occupying the periphery of the conglomerate mass, are lenticular and are far more cellular. Though all are rich in collagen, the fibres are more delicate. Central necrosis of a fibrinoid character is visible in six, and the general appearances in these are closely similar to those already noted in the pericardium. Several giant cells of Touton type are present in one of the remaining nodules, and in the compressed adjacent tissues of the dermis, which show a diffuse, mainly perivascular infiltration with lymphocytes, plasma cells, and large mononuclear cells. *A few of the giant cells unassociated with nodules are conspicuously foamy, but apart from these no foam cells are present.* The infiltration extends about the appendages to the deep borders of the overlying epidermis. The walls of blood vessels are unaltered.

In frozen sections the large hyaline nodules are for the most part devoid of Sudanophil material, but finely-granular aggregates occupy areas corresponding to the necrotic fibrinoid foci; they are associated with large, unstained acicular and rhomboid cholesterol crystals. In the smaller nodules the amount and distribution of Sudanophil lipoid corresponds to that already described for the pericardium.

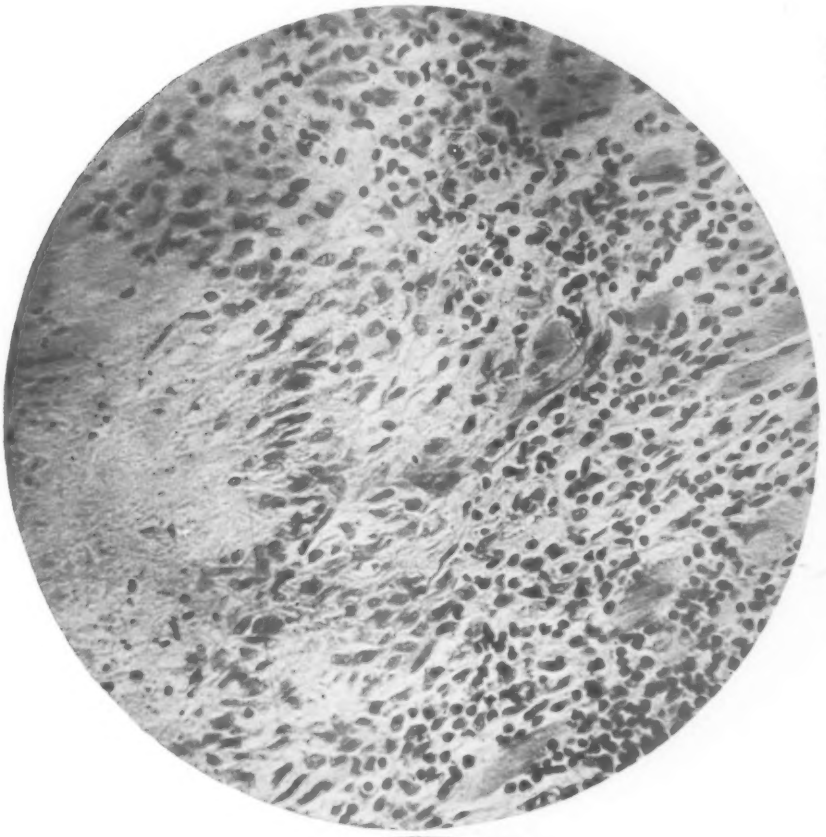


FIG. 2.—High-power view (×220) of part of Fig. 1. A typical necrobiotic focus in heart muscle. Note the clear, structureless zone. External to the latter the palisading of the nuclei and the cellular infiltration are well shown.

FIG. 1.—Low-power view (×45) of heart nodule, showing nuclear palisading and cellular infiltration external to the clear, structureless zone.

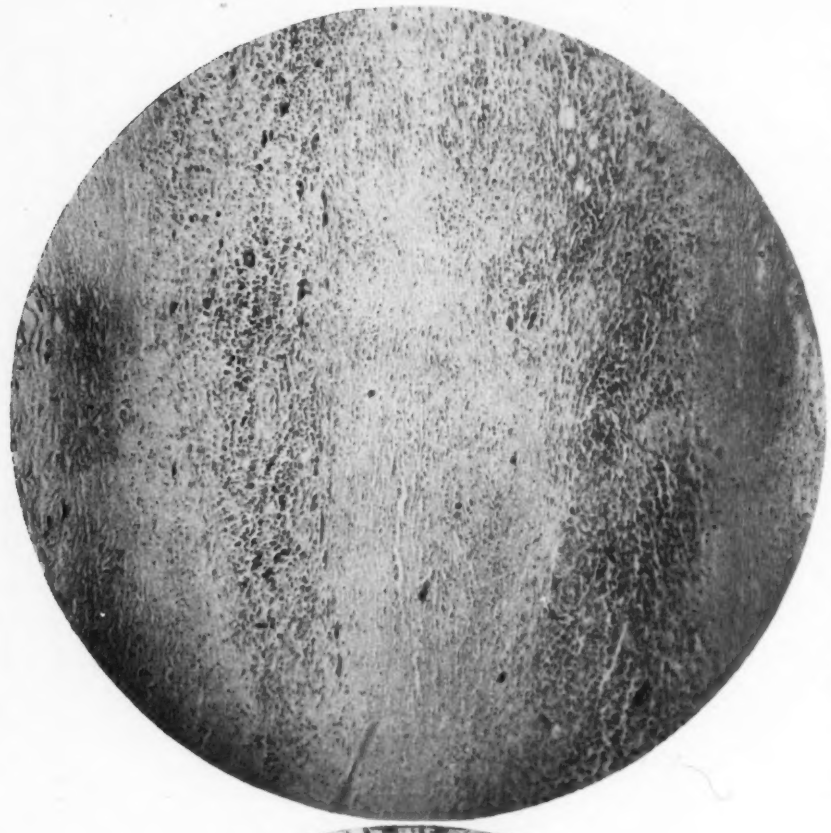
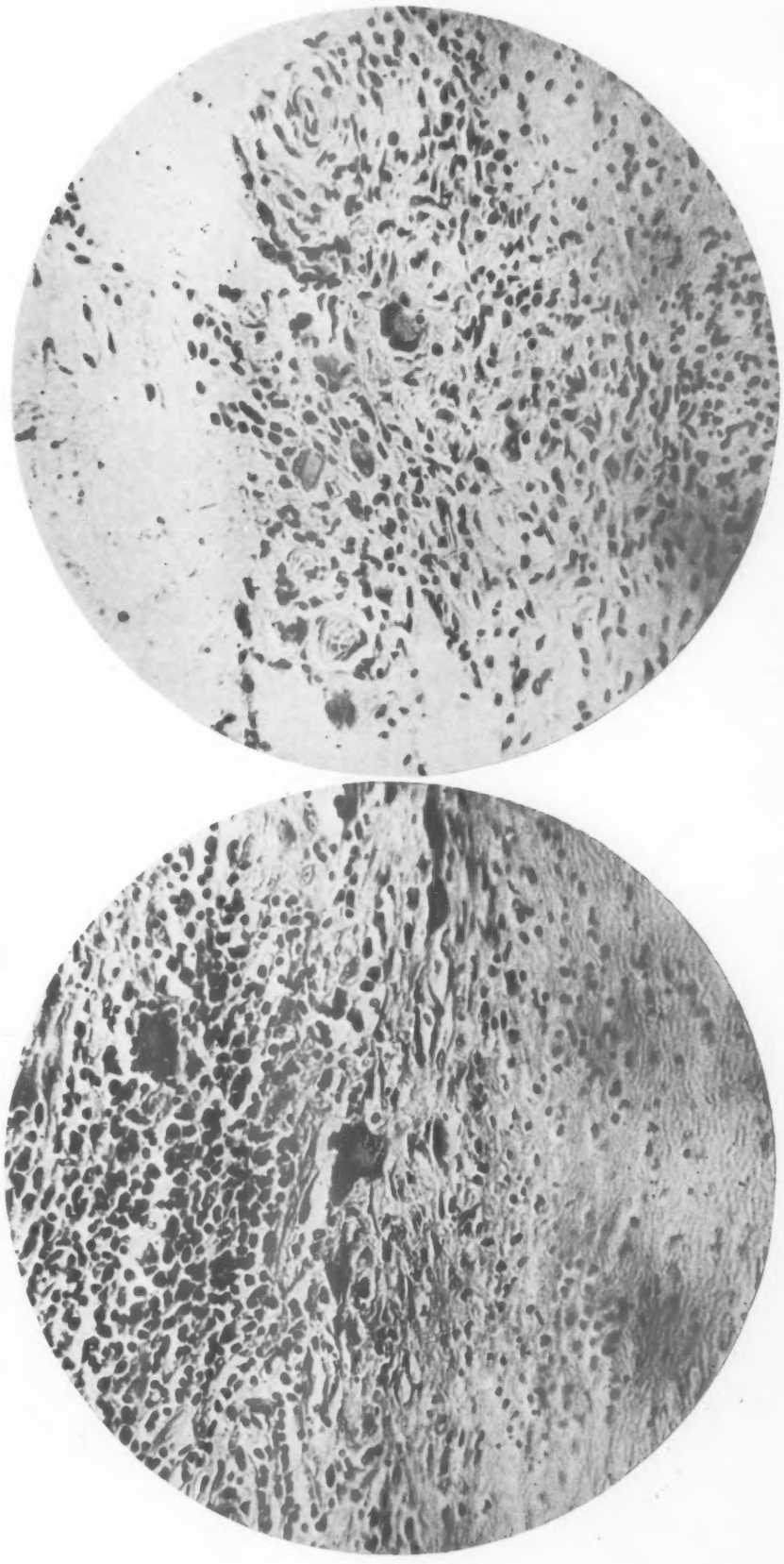


FIG. 4.—Confluent necrobiotic foci in heart muscle, showing giant cells. Low magnification (×45).

FIG. 3.—Multiple necrotic foci in the pleura. These lesions are at an earlier stage of development than those shown in Figs. 1 and 2 (×220).



FIGS. 5 and 6.—Showing typical multinucleated giant cells in heart lesions under high magnification (×220).

FIG. 8.—A focus of necrobiosis in pleura. Low magnification (×45).

FIG. 7.—Showing necrobiotic changes affecting fat and heart muscle. Low magnification (×45).

FIG. 9.—Nodules on the patient's forehead.

FIG. 10.—Nodules on the patient's abdomen.

FIG. 11.—Showing nodules on patient's right elbow and deformity of wrist.

FIG. 12.—Showing gross deformity of patient's left hand and wrist.

FIG. 13.—Radiograph showing gross deformity of left hand and wrist with osteoporosis.

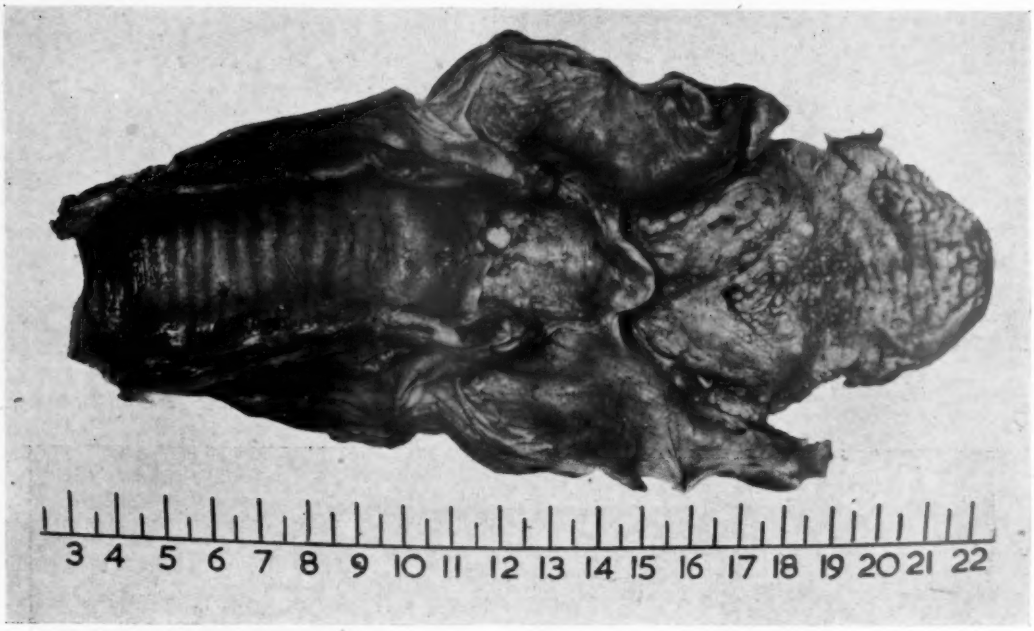


FIG. 14.—Showing small nodules in glottis, and particularly one rather larger one on the epiglottis

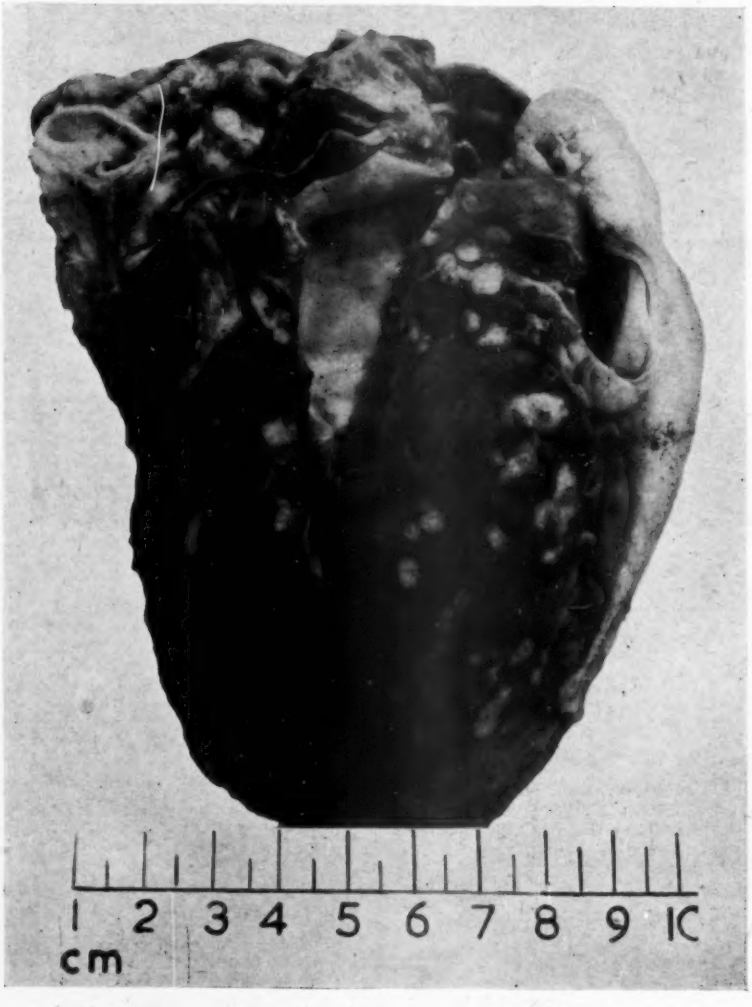


FIG. 15.—Heart, showing multiple epicardial nodules.

FIG. 16.—Nodule from larynx. Low power (×45). Several giant cells are discernible. Palisading indistinct.

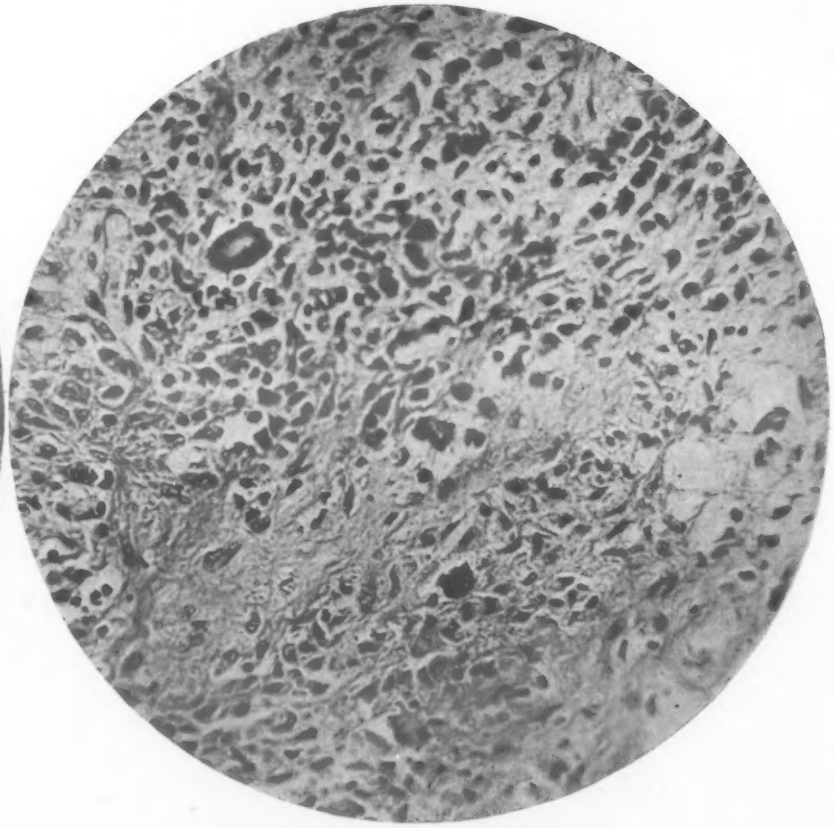


FIG. 17.—Part of Fig. 16 under high power (×220).

With polarized light there is abundant doubly refractive lipoid in the areas where crystals are present. Unfortunately few of the smaller peripheral nodules are represented; in those present the amount of doubly refractive lipoid appears somewhat greater than in the pericardial nodule."

Discussion

A case like our present one, in which the main feature during the latter part of the patient's life consisted in the almost universally distributed (both superficial and visceral) characteristic nodules of the rheumatoid arthritis type, makes one wonder whether rheumatoid arthritis should not be classified with the infective granulomata, together with tuberculosis, syphilis, and lepra, though the infective agent still remains unknown. A varying allergic-like reaction towards the infective agent (whatever it may be) almost certainly plays an important part in the symptomatology.

In regard to the involvement (in the present case) both of skeletal striped muscle (abdominal wall) and of heart muscle, it is interesting to study the paper by Steiner and others (1946) on " Lesions of Skeletal Muscles in Rheumatoid Arthritis". These authors describe a condition of " nodular polymyositis " in cases of rheumatoid arthritis, which, together with a kind of perineuritis, constitutes, they claim, an essential lesion in rheumatoid arthritis, for which they propose the term " nodular neuromyositis". The size of the nodules varied from those easily seen by naked-eye inspection in stained sections to very small (microscopic) ones. " Lymphocytes and plasma cells were abundant, mast cells occasional, and polymorphonuclear cells and eosinophils rare or absent." All the various lesions of rheumatoid arthritis they regard as of an inflammatory and granulomatous nature. The muscular lesions, they find, differ from those found in other diseases. They obviously differ in degree from the relatively gross necrobiotic nodules in our case.

As to the pericardial and heart lesions in the present case, one may remember that clinical signs of heart involvement of some kind are found in a great many cases of rheumatoid arthritis at various periods of the disease. Feiring (1945) reported an incidence of 29 per cent. (" carditis ") in twenty-seven cases of rheumatoid arthritis. It may be remembered that in Still's disease, which is an infantile or juvenile type of rheumatoid arthritis, Still himself reported the occurrence of pericarditis.

Incidentally, our case illustrates a point urged by Steiner and others (1946), namely, that in old quiescent and apparently " burnt-out " cases of rheumatoid arthritis one can never be sure that the disease may not burst out again with renewed virulence.

One may ask whether a case like the present may be related to certain rare conditions classed as examples of " disseminated lupus erythematosus ", a disease, according to Baehr and Pollack (1947), expressing itself morphologically as a fibrinoid degeneration of the collagen of the connective tissues. This, they say, " is but the structural symptom of the disease, whose essential nature is yet to be disclosed ". These authors speak of areas of fibrinoid degeneration in the subendothelial connective tissue of the epicardium, which are responsible for pericarditis; of the pleura, responsible for pleuritis; of the peritoneum, responsible for peri-splenitis or peri-hepatitis. In our present case we found no verrucose endocardial lesions of the so-called Libman type, nor the vascular lesions mentioned by these authors. Clinically, indeed, commencing dry gangrene of the right big toe was noted, but unfortunately the corresponding blood vessels were not examined post mortem.

Finally, in regard to lipoidal changes connected with the nodules, a lipoidosis of some kind may undoubtedly be associated with symptoms and lesions of rheumatoid arthritis. As in the present case and cases described by Fletcher (1946), and Kersley and others (1946), there may be, and probably usually is, lipoid material present in the necrobiotic nodules of rheumatoid arthritis type; Professor Russell is convinced that the sudanophil substances present in the nodules of our cases are no greater in amount, nor different in character, from what one might expect in such lesions with central necrosis. Secondly, there are rare cases which may be termed " lipoid rheumatism " or " xanthomatous rheumatism " (Parkes Weber and Freudenthal, 1937; Parkes Weber, 1943, and 1948; Layani, 1939; Layani and others, 1939). Graham and Stansfeld (1946) described an exceedingly puzzling case as one of " A Hitherto Undescribed Lipoidosis simulating Rheumatoid Arthritis ".

Addendum: January, 1948

Since this paper was completed, one of us (F. Parkes Weber), through the kindness of Dr. G. B. Dowling, has seen a middle-aged man with a typical nodular lesion over the left ulna, near the elbow, of the rheumatoid arthritis type. The patient likewise had a ringed swelling resembling granuloma annulare over the knuckle of the right index finger. This, like the elbow lesion, had gradually developed during the last two years. Both lesions were subcutaneous and situated over prominent bones, and both felt to palpation as if they consisted of multiple small nodules, each nodule probably representing a minute necrobiotic focus surrounded by an area of

CORRECTION

The paragraph after the summary does not belong to this paper. The following is to be substituted:

We have unfortunately overlooked the mention of a similar case of widely disseminated rheumatoid arthritis nodules with pericardial and pleural involvement (Bennett and others, loc. cit.).

inflammatory and fibroblastic reaction. There had also been pain in muscles and joints. Dr. Dowling had seen two similar cases, suggesting that at least some cases of granuloma annulare are of the same nature as the nodular lesions of rheumatoid arthritis, with a similar aetiological factor, not merely a histological resemblance. Even when characteristic arthritic symptoms are absent, nodules of the rheumatoid arthritis type and granuloma annulare may perhaps both be regarded as incomplete forms of what one might term the " rheumatoid arthritis syndrome ".

Summary

A case of rheumatoid arthritis is described, in which the characteristic necrobiotic nodules were of extensive distribution. Arthritis changes involved the joints of the arms and legs with gross deformity, and typical lesions were found in the larynx, in the muscles, and in the subcutaneous tissues. Moreover, the internal organs, including the lungs, pleurae, pericardium, and heart muscle, showed macroscopic nodules of characteristic histology.

Attention is drawn to the fact that some of the necrobiotic lesions were associated with giant cells, but that they were not universally present.

In regard to similar cases, which are likely sooner or later to be met with, it is hardly necessary to stress the importance of clinical estimation of phosphatase and phosphorus in the blood, and, if there should be a necropsy, the microscopical examination of the pituitary and parathyroid glands.

Our thanks are due to Mr. S. O. Aylett, F.R.C.S., Surgical Registrar to the Royal Cancer Hospital, for helpful suggestions; and to Professor Dorothy S. Russell, Pathologist to the London Hospital, for most valuable help in the histological examination of the nodules. We also thank Miss Hunt for the clinical photographs; Mr. Chadwin for histological preparations; and Mr. Cowles for photomicrographs.

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Les Nodules Necrobiotiques dans l'Arthrite Rhumatismale

Résumé

Cet article décrit un cas d'arthrite rhumatismale dans laquelle les nodules nécrobiotiques étaient très largement distribués. Les modifications arthritiques atteignaient les articulations des bras et des jambes qui présentaient des déformations importantes, et l'on a trouvé des lésions caractéristiques dans le larynx, dans les muscles, et dans les tissus sous-cutanés. De plus les organes internes, y compris les poumons, les plèvres, le péricarde et le muscle cardiaque présentaient des nodules macroscopiques caractéristiques histologiquement.

On attire l'attention sur le fait que les lésions nécrobiotiques étaient associées avec des cellules géantes, mais qu'elles n'étaient pas présentes partout.

INVESTIGATIONS INTO THE EFFECT OF HOT, DRY MICROCLIMATE ON PERIPHERAL CIRCULATION, ETC., IN ARTHRITIC PATIENTS

BY

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During the last six years one of the wards of the University Hospital in Lund has been used as a climatic laboratory. The temperature of the air in the room can be adjusted between what is normal outdoor temperature in south Sweden—in the winter below zero—and 40° C., the relative humidity between 30 per cent. and complete saturation, and both these factors can be kept constant at the level desired with a very small range of variation.

The Arrangement of the Ward

No expensive arrangements have been made. An ordinary sick ward with space for two beds has been provided with double walls, double ceilings and double floors, with free air-space between the two layers. The old double window has been furnished with another two inner sashes. The space between the old door of the room and that built in the new wall has been arranged as an air-lock, where the staff and the visitors stop for a while to regulate the temperature of their clothes before entering the ward.

The air-jacket within the double walls, sashes, floors, and ceilings, and the air in the lock, are electrically heated to the required temperature and set in motion by a fan.

The air for the laboratory itself is drawn through an air-conditioning plant in the corridor outside the room; it is blown into the laboratory through a central grating in the inner ceiling, surplus air being afterwards pressed out of the room through exhaust conduits that run round the edge of the inner ceiling.

If the regulating thermostats—one for the air jacket, the other for the air of the room—are set at the same temperature, which has always been done in these investigations, the result will be absence of convection currents and very little air movement in the lower part of the room. So-called draughts will be entirely excluded.

The relative air humidity in the room is adjusted by means of a psychrostat. (For a more detailed description, see Edström, 1944.)

The Tolerated Temperature

After a period of testing to see how the patients would tolerate different temperatures and humidities, we came to the same result as Gagge and others (1937), viz. that 32° C. (89·6° F.) was agreeable and that under this temperature the patients were not troubled by any perspiration worth mentioning if the relative humidity of the air was kept below 50 per cent. In the subsequent tests we accordingly stopped at a temperature of 32° C. and a relative humidity of 35 per cent. Under these circumstances sixteen patients with rheumatic fever in a rather late stage, and eighteen patients with rheumatoid arthritis have been treated, each of them for about a hundred days on an average.

The Investigation

The effects on these patients of their stay in this dry, hot microclimate for so long a time—they were not allowed to leave the room during the whole of their stay in the " laboratory "—were then investigated.

The skin temperature of the patients was determined with a thermo-couple of copper and constantan. At the soldered joint intended for application to the skin the filaments intersected one another at right angles. At the intersection they were soldered. This soldered junction was exactly in the middle of a ring of ebonite, the upper part of which was continued in a handle of ebonite. The second soldered joint, which during the investigations should be at a constant known temperature, was fixed at the mercury-receptacle of a mercury-thermometer having 0·05° C. graduations and placed in a thermos flask containing water at about 30° C. (86° F.) For registration of the electromotive power a multiflex galvanometer was used, so graduated that every line on the scale corresponded to 0·05° C., which was controlled by repeated calibrations. When measurements were

being taken the thermo-couple was always placed on the skin for exactly ten seconds.

As a rule, at every investigation the skin temperature was measured once a minute, at least five times, on the following parts of the body: the volar side of the distal phalanx of the thumb, the middle of the dorsal side of the upper arm, and the middle of the soft part of the cheek. The thermo-couple was placed exactly on the same place and under the same pressure at every measuring (Ipsen, 1936). When the effect of cold was being studied one of the hands of the patient was placed in ice-water. When the effect of amyl nitrite was being studied the patient inhaled this substance.

For determining the oxygen content of the blood van Slyke and Neill's monometric method was employed (van Slyke and Neill, 1924; Edström, 1943). Measurement of the cardiac output was done by the acetylene method (Grollman, 1932). For the determination of the basal metabolic rate the method with a Douglas bag was used (Douglas, 1911).

All these determinations were carried out at eight o'clock in the morning, immediately after the patients had awakened and while they were still resting and had not had anything to eat or drink.

Results

It is evident from the investigation that, under an ordinary room temperature of 20° C. and a normal relative humidity of the air of about 50 to 60 per cent., these patients in hospital—especially most cases of rheumatoid arthritis—show a relatively low skin-temperature on the distal parts of the extremities —lower than that of normal healthy persons (Edström, 1940 ; Wright and Pemberton, 1930)—and that the difference between the skin-temperature of these parts and of the trunk is very high (Tables 1 and 2, Figs. 1, 2, and 3).

TABLE 1

THE ARITHMETIC MEAN OF TEMPERATURE READINGS ON THE THUMB BEFORE AND DURING TREATMENT IN THE CLIMATIC LABORATORY

Patient	Before (°C.)	During (°C.)
1	29·2 ± 0·6	32·9 ± 0·3
2	30·8 ± 0·3	33·0 ± 0·2
3	30·5 ± 0·8	35·1 ± 0·5
4	29·1 ± 0·2	35·2 ± 0·2
5	29·6 ± 0·2	35·3 ± 0·1
6	28·0 ± 0·6	32·1 ± 0·2
7	31·5 ± 0·8	34·1 ± 0·6
8	27·0 ± 0·3	33·9 ± 0·5
9	26·8 ± 0·4	32·8 ± 0·2
10	30·1 ± 0·3	35·1 ± 0·2

The arithmetic mean of all readings of all patients:
Before treatment in the climatic laboratory: 28·9 ± 0·4.
During treatment in the climatic laboratory: 34·0 ± 0·3.
Difference: 5·1 ± 0·5.

TABLE 2

THE ARITHMETIC MEAN OF TEMPERATURE READINGS ON THE UPPER ARM BEFORE AND DURING TREATMENT IN THE CLIMATIC LABORATORY

Patient	Before (°C.)	During (°C.)
1	30·3 ± 0·3	33·4 ± 0·3
2	30·5 ± 0·3	31·6 ± 0·3
3	30·0 ± 0·2	34·4 ± 0·2
4	30·0 ± 0·3	33·8 ± 0·2
5	31·3 ± 0·1	34·7 ± 0·1
6	31·0 ± 0·5	32·1 ± 0·4
7	31·1 ± 0·8	33·7 ± 0·8
8	28·3 ± 0·9	34·1 ± 0·2
9	31·8 ± 0·3	31·3 ± 0·2
10	31·6 ± 0·4	35·1 ± 0·2

The arithmetic mean of all readings of all patients:
Before treatment in the climatic laboratory: 30·6 ± 0·4.
During treatment in the climatic laboratory: 33·4 ± 0·3.
Difference: 2·8 ± 0·5.
Difference between the increase of temperature of the thumb and the upper arm during the treatment in the climatic laboratory: 2·3 ± 0·7.

In the hot-room this skin-temperature rose, though much more on hands, feet, and distal parts of the extremities (just as far as the effect of the arterio-venous anastomosis reaches) than on the trunk, so that the difference has been inverted, warmer skin-temperature occurring on the distal parts than on the central. The peripheral vasospasm has been converted into peripheral vasodilatation. The peripheral circulation has increased, and the arteriovenous anastomoses especially have been maximally dilated.

A very interesting point is that, besides the consensual reaction of the vessels against, for example, ice on the skin, the inhalation of amyl nitrite, etc., in the warm-room is lowered or in some cases is inhibited (Tables 3 and 4, Figs. 4 and 5). The effect of the relative oxygen saturation of venous blood runs a parallel course.

At an ordinary room temperature of 20° C. oxygen unsaturation of venous blood, measured at the median cubital vein, was, on an average of 12 patients in 20 determinations, 8·22 vol. per cent. ±1·11, or 51 per cent. mean oxygen saturation. That is a low saturation. In normal individuals Lundsgaard (1918) found an oxygen saturation of 68 per cent. under the same conditions, and several other authors have found values that have also been around 70 per cent. (Liljestrand, 1928). This relatively low oxygen saturation in the venous blood can no doubt also be considered in association with the constricted peripheral circulation in these arthritic patients (Fig. 6).

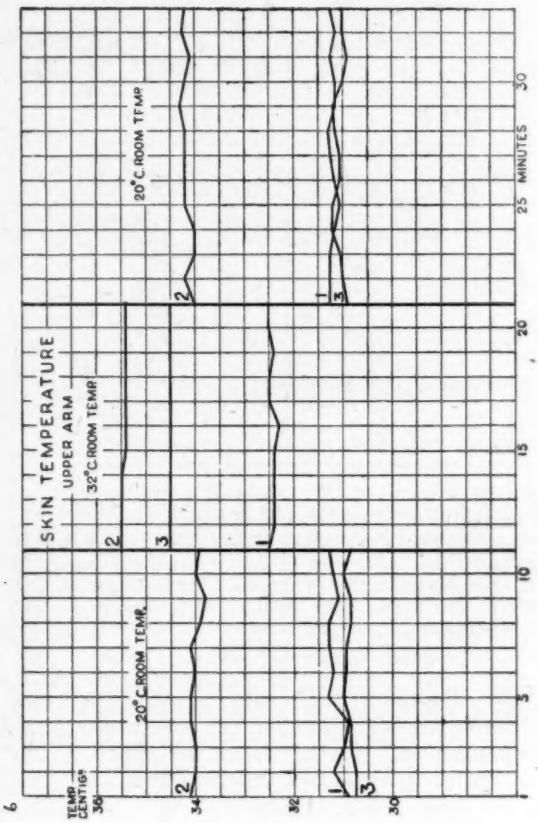

FIG. 2.

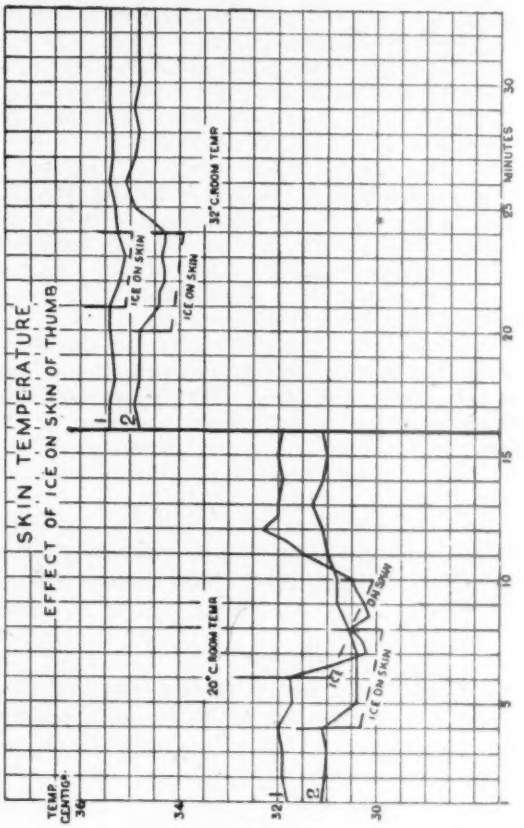

FIG. 4.

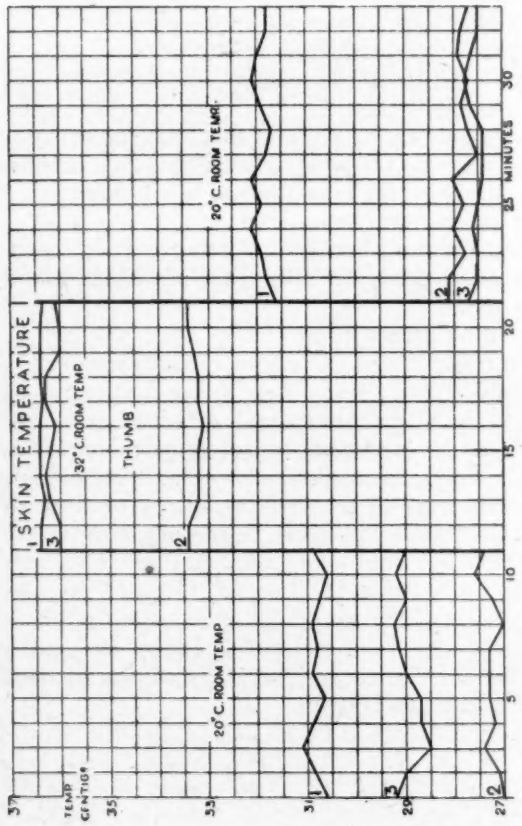

FIG. 1.

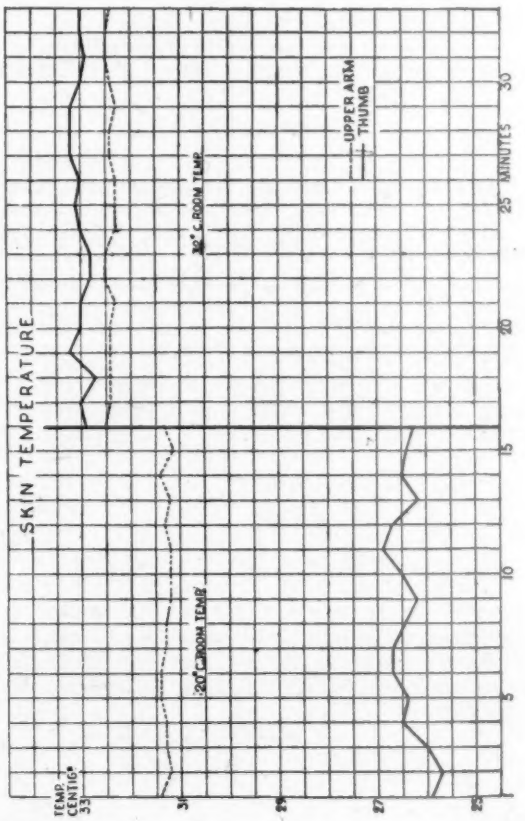

FIG. 3.

TABLE 3

INFLUENCE UPON THE TEMPERATURE OF ONE THUMB WHEN COOLING THE OTHER HAND IN ICE WATER BEFORE AND DURING THE TREATMENT IN THE CLIMATIC LABORATORY

Patient	Before (°C.)	During (°C.)
1	− 0·9 ± 0·04	− 0·1 ± 0·09
2	− 0·3 ± 0·09	− 0·0 ± 0·03
3	− 0·2 ± 0·05	− 0·0 ± 0·03
4	− 0·7 ± 0·09	− 0·1 ± 0·06
5	− 0·7 ± 0·06	− 0·3 ± 0·07
6	− 1·0 ± 0·12	− 0·2 ± 0·06
7	− 0·6 ± 0·06	− 0·0 ± 0·03
8	− 0·7 ± 0·06	− 0·0 ± 0·03
9	− 0·9 ± 0·06	− 0·1 ± 0·03
10	− 1·1 ± 0·06	− 0·0 ± 0·05

The arithmetic mean of all the readings :
Alteration of temperature before treatment in the climatic laboratory : − 0·7 ± 0·07.
Alteration of temperature during treatment in the climatic laboratory: − 0·1 ± 0·06.
Difference: 0·6 ± 0·06.

TABLE 4

INFLUENCE UPON THE TEMPERATURE OF THE THUMB OF INHALATION OF AMYL NITRITE BEFORE AND DURING TREATMENT IN THE CLIMATIC LABORATORY

Patient	Before (°C.)	During (°C.)
3	− 1·2 ± 0·16	− 0·1 ± 0·06
4	− 0·3 ± 0·08	− 0·0 ± 0·00
5	− 0·1 ± 0·03	− 0·1 ± 0·02
6	− 0·9 ± 0·17	− 0·0 ± 0·06
7	− 1·2 ± 0·28	− 0·2 ± 0·08
8	− 0·9 ± 0·12	− 0·1 ± 0·01
9	− 0·6 ± 0·22	− 0·2 ± 0·06

The arithmetic mean of all the readings:
Alteration of the temperature before treatment in the climatic laboratory: 0·7 ± 0·15.
Alteration of the temperature during treatment in the climatic laboratory: 0·1 ± 0·04.
Difference: 0·6 ± 0·15.

At a room temperature of 32° C. we found on an average of 6 patients in 24 determinations 2·92 vol. per cent. ±0·62 or 82 per cent. mean oxygen saturation (Edström, 1943). Goldschmidt and Light had observed that by keeping the forearm in hot water at a temperature of about 45° C. a relative oxygen saturation could be established in the venous blood, measured in the same way in the cubital vein, of up to 92 per cent., that is, a value bordering on that of the arterial blood. By keeping the forearm in water at a temperature between 29° and 39° C. the authors were not able to obtain a higher oxygen saturation in these veins than 69 per cent., and by keeping it in air up to 32° C., at most 75 per cent. The difference lies in the length of stay in the room, and also in the constancy of the temperature, this being the reason that a stronger effect was obtained by us.

The abnormally low saturation of the venous blood in these arthritic patients seems also to be a sign of the peripheral vasospasm. When this spasm vanished in the hot-room and was converted into vasodilatation, the saturation was good, and it seems that this maximal dilatation of the arterio-venous anastomoses is the reason for so high an oxygen saturation, approximating to the saturation of the arterial blood.

The venous blood taken from the cubital vein in the hot-room had a bright red colour which was at once noticeable, this being an observation similar to one made by many physicians in the tropics. This colour is caused by the high oxygen saturation of the blood, and we can thus confirm Mayer's hundred-year-old assumption. The haemoglobin was unchanged.

The cardiac output per minute (Table 5) was investigated before, during, and after the stay in the room. At normal heart function there were no statistically significant changes in it (Edström, 1944). In some cases with cardiac defect we obtained good compensating effect from the stay in the hot-room. It seems to be the diminished active peripheral resistance to blood flow at this higher temperature that is here of first importance (Wezler and Thauer, 1942).

Broadly speaking, no changes in calorie consumption and basal metabolic rate have been observed. However, there have been some individual variations (Edström, 1944) (Table 6, Fig. 7).

Thus, the so-called second chemical regulation of body-temperature has not begun to function at this temperature of 32° C., at any rate in the majority of cases.

Cultures from the throat flora were regularly taken from all patients. In 24 of them (11 of the rheumatic-fever cases and 13 of the rheumatoid-arthritis cases) these cultures on admission of the patients to the laboratory have shown β-haemolytic streptococci. In 22 of these, the cocci disappeared during the stay in the hot-room. Corresponding results have been obtained by removing persons from a temperate to a tropical climate (Coburn, 1931).

All cases treated in the laboratory were severe ones which had not improved earlier under ordinary internal and physical therapy.

The most obvious effects on the clinical symptoms were: remission of the periarticular oedema and

TABLE 5

THE CARDIAC OUTPUT PER MINUTE BEFORE AND DURING TREATMENT IN THE CLIMATIC LABORATORY

Patient	Before (litres)	During (litres)
4	4·6 ± 0·6	4·3 ± 0·2
5	4·9 ± 0·6	4·8 ± 0·6
6	3·8 ± 0·2	4·1 ± 0·2
7	5·1 ± 0·2	4·5 ± 0·4
8	5·1 ± 0·1	4·8 ± 0·2
9	3·6 ± 0·2	3·9 ± 0·2
10	3·5 ± 0·2	3·0 ± 0·0

The arithmetic mean of all the readings:
Before treatment in the climatic laboratory: 4·4 ± 0·3 litres
During treatment in the climatic laboratory: 4·3 ± 0·3 litres.
Difference: 0·1 ± 0·4 litres.

TABLE 6

THE BASAL METABOLISM BEFORE AND DURING TREATMENT IN THE CLIMATIC LABORATORY

Patient	Before (calories)	During (calories)
4	1·03 ± 0·08	0·95 ± 0·05
5	0·94 ± 0·00	0·89 ± 0·04
6	0·97 ± 0·04	0·92 ± 0·06
7	1·12 ± 0·07	1·18 ± 0·02
8	1·13 ± 0·03	1·13 ± 0·01
9	0·92 ± 0·03	1·04 ± 0·02
10	1·03 ± 0·01	1·07 ± 0·03

The arithmetic mean of all the readings:
Before treatment in the climatic laboratory: 1·02 ± 0·04 cal.
During treatment in the climatic laboratory: 1·03 ± 0·03 cal.
Difference: 0·01 ± 0·05 cal.

the capsular swelling of the attacked joints, diminished shifting pains and contractures; after some days in the hot-room the patients could walk and move about much better and more easily, they had a larger appetite, and their weight went up; they had improved function in cases of cardiac defect, and the blue-livid coloration of the skin on hands and feet vanished.

Of the 16 rheumatic-fever cases, 13 improved, became entirely free from symptoms, and are at times capable of working. Ten of them, however, have deformities of their mitral valves. Two died of heart failure, and one of nephritis and uraemia.

Of the 18 rheumatoid arthritis cases, 8 became free from clinical symptoms and are at times entirely capable of work. Six improved, and 4 of these are at times working and in good condition; 2 had recurrence respectively one and a half and three years after treatment in the warm-room. Two cases improved temporarily but deteriorated again. One case improved during the first treatment but had a relapse after return home four months later and could not be influenced by renewed treatment in the ward. In one case the treatment was broken off.

Tendency to recurrence immediately after removal back to ordinary room temperature was in no case observed.

Thus, there are three things we have especially found to result from the stay of the patients in the dry, hot microclimate: changes in peripheral circulation, changes in oxygen saturation of the venous blood, and changes in the throat flora. It seems as if the bacteriological changes are the results of the physiological. From the observations made we can begin to understand why β-haemolytic streptococci in throat flora, and diseases caused by such streptococci are relatively uncommon in tropical climates. I say "tropical climate" and not "the tropics" since it is the climate and not the latitude that is of importance.

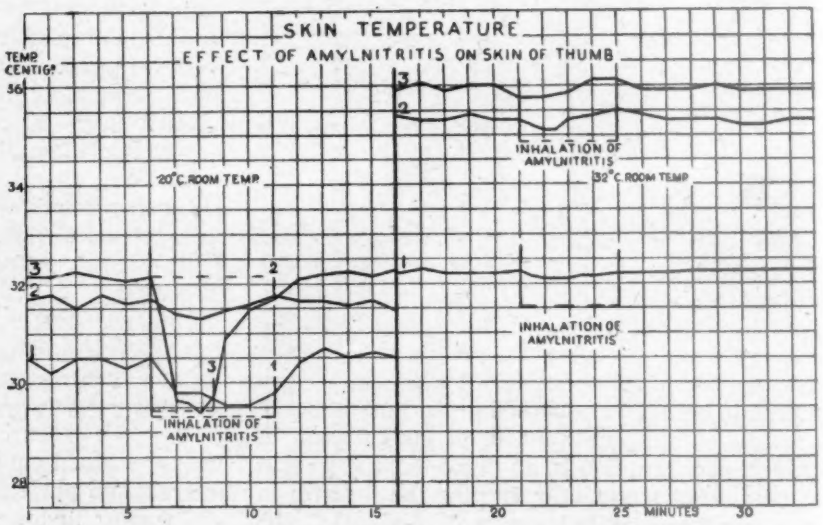

FIG. 5.

Summary

For the last six years we have had one ward in the Rheumatological Department of the University

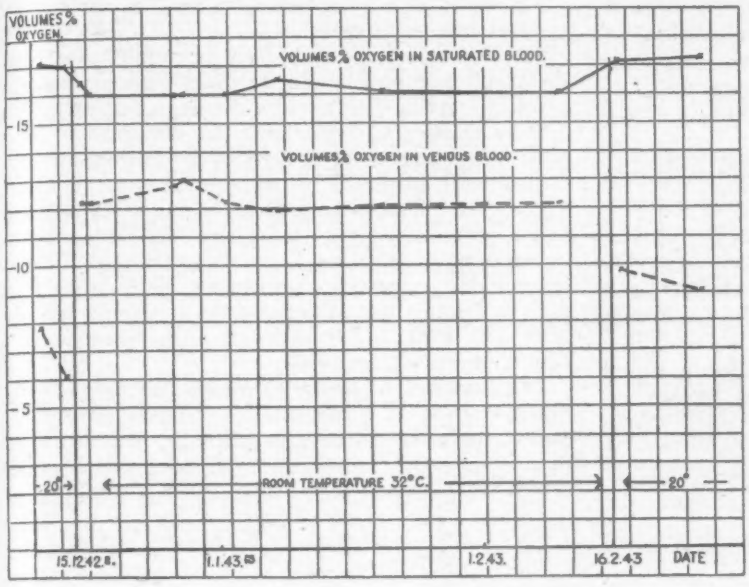

FIG. 6.

Hospital in Lund constantly air-conditioned at 32° C. and 35 per cent. relative humidity. In this ward we have treated arthritic patients, each of them for about a hundred days on an average.

The effect of the hot, dry microclimate on these patients is as follows:

1. The peripheral circulation increased in all. Peripheral vasospasm was converted into peripheral vasodilatation. The arteriovenous anastomoses especially have been maximally dilated. The temperature of the skin, which was lower at an ordinary room temperature of 20° C. (especially in cases of rheumatoid arthritis) has been raised, particularly on hands, feet, and distal parts of the extremities, so far as the effect of the anastomoses has reached, where it has been higher than on more proximal parts on the trunk. In addition the consensual reaction of the vessels against, for example, ice on the skin, inhalation of amyl nitrite, etc., was lowered or failed to appear.

2. The relative oxygen saturation of venous blood, measured at the medial cubital vein increased in the hot-room, while the arteriovenous difference diminished. At a room temperature of 20° C. we obtained a 51 per cent. mean oxygen saturation, a very low saturation that can be considered in association with the constricted peripheral circulation in these patients also. In the hot-room the result was 82 per cent. mean oxygen saturation. Thus we may say that the bright red colour of venous blood in the tropics is caused by the high oxygen saturation of the blood. The haemoglobin was unchanged.

3. The cardiac output per minute showed no statistically significant changes in cases of normal heart function. In cases with cardiac defect the function of the heart was better, probably owing to a diminished active peripheral resistance to blood flow at the higher temperature.

4. In most cases no changes in calorie consumption and basal metabolic rate could be observed. Thus, the so-called second chemical regulation of body temperature had not entered into function at this temperature of 32° C. at any rate in the majority of cases.

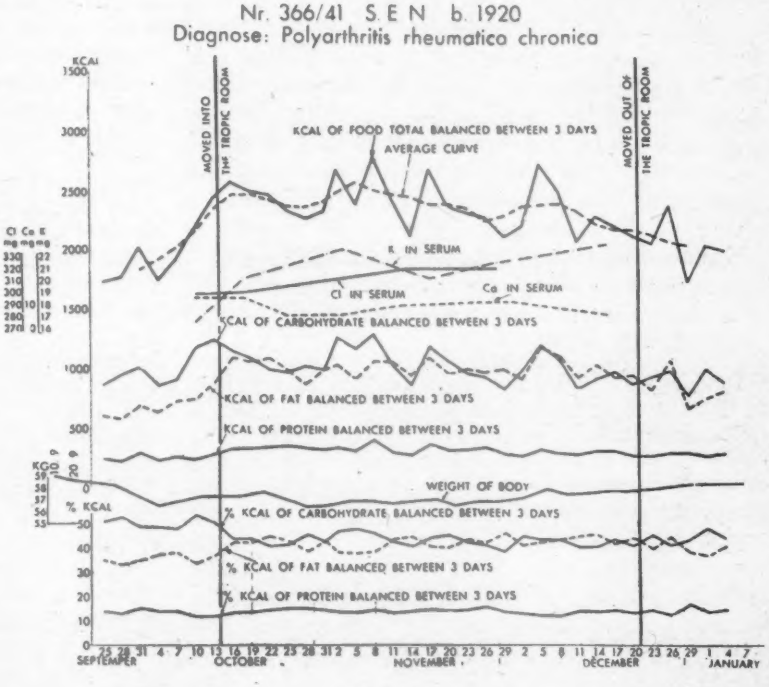

FIG. 7.

5. Cultures from the throat flora showed in most cases β-haemolytic streptococci on admission of patients to the hot-room, but only in two cases were such cocci detected at the end of their stay. It seems as if these cocci do not tolerate this dry, hot climate in the room.

6. The most obvious effects on the clinical symptoms have been: remission of periarticular oedema and capsular swelling of attacked joints, diminished shifting pains and contractures, better appetite, improved function in cases of cardiac defects, and disappearance of the blue-livid coloration of skin on hands and feet.

Tendency to recurrence immediately after removal back into ordinary room temperature has in no case been observed.

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Examination des Effets du Microclimat Chaud et Sec sur les Malades Arthritiques, leur Circulation Périphérique, etc.

Résumé

Pendant les six dernières années une salle de la section de Rhumatologie de l'Hôpital de l'Université de Lund, a été constamment maintenue par conditionnement de l'air à 32° C et à 35 pour cent d'humidité relative. Dans cette salle nous avons traité des malades arthritiques, chacun d'eux pendant une durée moyenne de cent jours environ.

Les effets de ce microclimat chaud et sec sur ces malades sont les suivants:

1. La circulation périphérique augmente chez tous. Le vasospasme périphérique se transforme en vasodilatation. Les anastomoses artérioveineuses en particulier ont été dilatées au maximum. La température de la peau qui (particulièrement dans les cas d'arthrite rhumatismale) était basse à la température moyenne de 20° C, s'est élevée, notamment pour les mains et les pieds, et les extrémités distales, aussi loin que l'action des anastomoses avait pu atteindre, là où elle avait été plus élevée que sur les parties plus proximales sur le tronc. De plus, la réaction des vaisseaux à des stimulants tels que glace sur la peau, inhalation de nitrite d'amyle, etc., était diminuée ou supprimée.

2. La saturation relative en oxygène du sang veineux, mesurée dans la veine cubitale, augmentait dans la salle chaude, tandis que la différence artérioveineuse diminuait. Dans une salle à 20° C nous obtenions une saturation moyenne de 51 pour cent, saturation très faible qui peut être considérée comme due à la vasoconstriction périphérique de ces malades. Dans la salle chaude le résultat était de 82 pour cent de saturation en oxygène. Nous pouvons donc dire que la coloration rouge vif du sang veineux sous les tropiques est due à la saturation élevée du sang en oxygène. L'hémoglobine n'était pas modifiée.

3. Le débit cardiaque par minute ne présentait aucune modification statistiquement significative dans les cas de fonctionnement normal du coeur. En cas de troubles cardiaques il y avait une amélioration due probablement à la diminution de la résistance périphérique active au flux sanguin à cette température élevée.

4. Dans la plupart des cas on n'a observé aucune modification dans la consommation en calories ou le métabolisme basal. Les soi-disant mécanismes de régulations chimiques secondaires de la température corporelle n'étaient pas entrés en jeu à cette température de 32° C, du moins dans la majorité des cas.

5. Des cultures de la flore pharyngée présentèrent dans la plupart des cas du streptocoque hémolytique β au moment de l'admission des malades dans la salle chaude, mais dans deux cas seulement ces cocci étaient encore présents à la fin du séjour. Il semble que ces cocci ne supportent pas l'atmosphère chaude et sèche de cette pièce.

6. Les effets les plus marqués sur les symptomes cliniques ont été: l'amélioration de l'oedème périarticulaire et de l'enflûre capsulaire des articulations atteintes, la diminution des douleurs fulgurantes et des contractures, l'amélioration de l'appétit, une amélioration fonctionnelle dans les cas de troubles cardiaques, et la diminution de la cyanose des extrémités.

On n'a observé dans aucun cas de tendance à la rechute aussitôt aprés le retour dans une salle à température normale.

FLOCCULATION TESTS IN RHEUMATOID ARTHRITIS

BY

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In addition to specific liver function tests, such as the synthesis of hippuric acid, laevulose tolerance and excretion of dyes, empirical tests have been devised which all depend mainly on excess of gamma-globulin in the serum (Gray, 1942; Kabat and others, 1943). The original object of these tests was threefold: (1) to distinguish between jaundice due to hepatitis and that due to obstruction of the bile-ducts; (2) to assist in the diagnosis of hepatitis in the early pre-icteric stage; and (3) to follow the course of hepatitis and aid in its prognosis. Two of these empirical tests—serum colloidal gold and cephalin-cholesterol flocculation—have been found to be particularly sensitive in parenchymatous disease of the liver.

According to Gray (1942), the foundation for the diagnostic use of the colloidal gold reaction was laid by Zsigmondy (1901), who observed that certain colloids, especially proteins, prevented the precipitation of colloidal gold suspensions by electrolytes. Lange (1912) found, however, that proteins within certain dilutions did not prevent but actually caused precipitation. Sweet and others (1941) pointed out that when a colloidal gold suspension is added to certain dilutions of blood serum from patients with liver disease flocculation of the colloidal gold occurs in one or more of the first serial dilutions. Gray (1942) performed a series of electrophoretic studies on the serum proteins in all types of liver disease, which revealed that the most characteristic and consistent alteration of the serum proteins was an increase in the gamma-globulin associated with a decrease in albumin. He then studied the effect on the colloidal gold solution of the addition of purified protein fractions to normal serum and obtained the following results:

(a) the addition of pure gamma-globulin to normal blood serum gave a positive colloidal gold reaction;
(b) the purified fractions with alpha- and beta-globulin had no effect;
(c) the albumin fraction inhibited the serum colloidal gold reaction.

As the result of these findings Gray suggested that the mechanism of the serum colloidal gold reaction in liver disease depended upon a relative increase in the gamma-globulin of the blood.

According to Maclagan (1944), Gray's original description of the serum colloidal gold reaction presented certain difficulties, including standardization of the solution. Moreover, while the test gave positive results in 100 per cent. of cases of cirrhosis of the liver, it was also positive in 10 per cent. of normal subjects. To overcome these difficulties, Maclagan devised a modification of Gray's test; this was simpler to perform, requiring only one tube instead of ten. The sensitivity of the reaction in cirrhosis of the liver and hepatitis was unimpaired, and normal subjects gave uniformly negative results.

While the principal use of the serum colloidal gold reaction was in diseases of the liver, it was soon found that positive results were obtained in certain non-hepatic diseases such as malaria, glandular fever, subacute bacterial endocarditis, and rheumatoid arthritis. Carter and Maclagan (1946) found that the test was positive in 76 per cent. of a series of thirty-four patients with rheumatoid arthritis, the results varying from mild to strongly positive.

The cephalin-cholesterol flocculation reaction was first introduced by Hanger (1939) as a test of hepatic efficiency, and was shown by several American workers (Hanger, 1939; Pohle and Stewart, 1941; and Mateer and others, 1942) to be extremely sensitive in the early detection of liver insufficiency. Like the serum colloidal gold reaction it, too, gives positive results with non-hepatic diseases including rheumatoid arthritis. The percentage of positive reactions in the latter disease, however, has been small. Dick (1945) obtained complete flocculation in only two out of forty-one patients with rheumatoid arthritis, the remaining thirty-nine failing to show any flocculation. Maizels (1946) noted a weakly positive result in one out of five cases of rheumatoid arthritis.

The present investigation was undertaken in

order to determine whether either of the flocculation tests, more particularly the serum colloidal gold reaction, might be of value, not as a diagnostic test as in liver diseases, but as an indicator of the activity or a guide in the prognosis of rheumatoid arthritis. Although the work of Carter and Maclagan (1946) gave promising results, it was felt that a larger series of cases was necessary before any definite opinion could be formed about the value of the serum colloidal gold reaction. In addition, an opportunity was afforded for comparing the results of the flocculation tests with the plasma proteins, erythrocyte sedimentation rate, and other clinical findings.

Maclagan's modification of Gray's serum colloidal gold test and Hanger's cephalin-cholesterol flocculation test were used throughout the investigation.

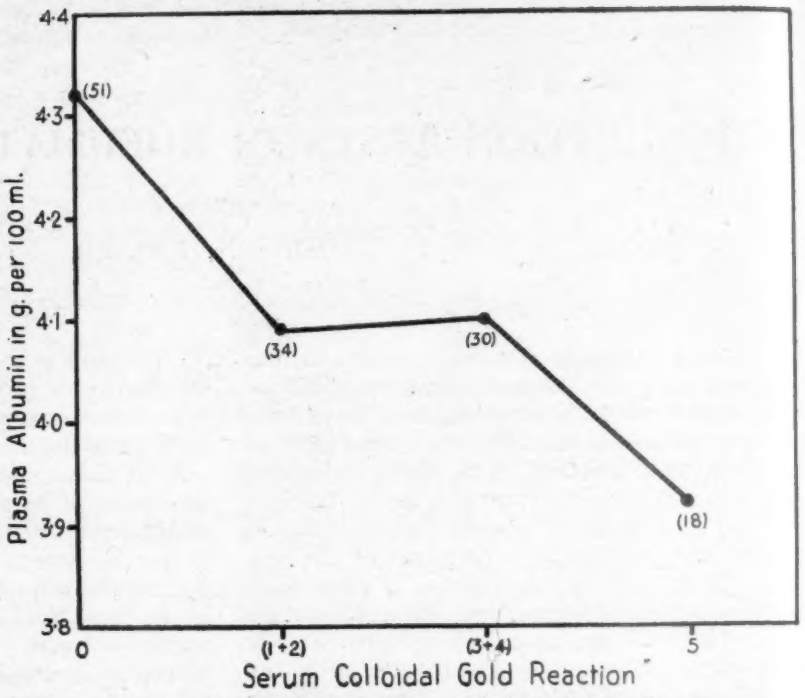

FIG. 1.—Serum colloidal gold reaction and plasma albumin (number of observations shown in brackets).

Results

Normal Controls.—The serum colloidal gold and cephalin-cholesterol flocculation tests were performed on one hundred healthy blood donors with uniformly negative results.

Rheumatoid Arthritis.—One hundred and thirty-three observations with the serum colloidal gold and cephalin-cholesterol flocculation tests were made on a hundred patients suffering from rheumatoid arthritis. Sixty-one per cent. of the former and 19 per cent. of the latter were found to be positive (Table 1). In addition, it was found that in 17 per cent. both tests were positive.

TABLE 1

SERUM COLLOIDAL GOLD AND CEPHALIN-CHOLESTEROL FLOCCULATION TESTS IN RHEUMATOID ARTHRITIS

(133 Observations on 100 Cases)

	No. of observations	Positive	
		No.	%
Colloidal gold	133	81	61
Cephalin-cholesterol ..	133	25	19
Both tests	133	22	17

Table 2 shows the degree of flocculation present in both tests. It will be seen that complete flocculation was obtained in 18 instances in the case of the serum colloidal gold reaction and in only 5 in the cephalin-cholesterol flocculation test.

TABLE 2

DEGREE OF FLOCCULATION OF SERUM COLLOIDAL GOLD AND CEPHALIN-CHOLESTEROL TESTS IN RHEUMATOID ARTHRITIS

(133 Observations on 100 Cases)

Cephalin-cholesterol	Colloidal gold						
	0	1+	2+	3+	4+	5+	Totals
0	49	16	9	8	16	10	108
+	1	2	1	1	1	2	8
++	0	1	0	1	0	2	4
+++	1	3	0	0	2	2	8
++++	1	1	0	0	1	2	5
Totals ..	52	23	10	10	20	18	133

An attempt was made to see if the flocculation tests showed any correlation with various factors.

Plasma proteins.—The results of the two flocculation tests were compared with the total plasma

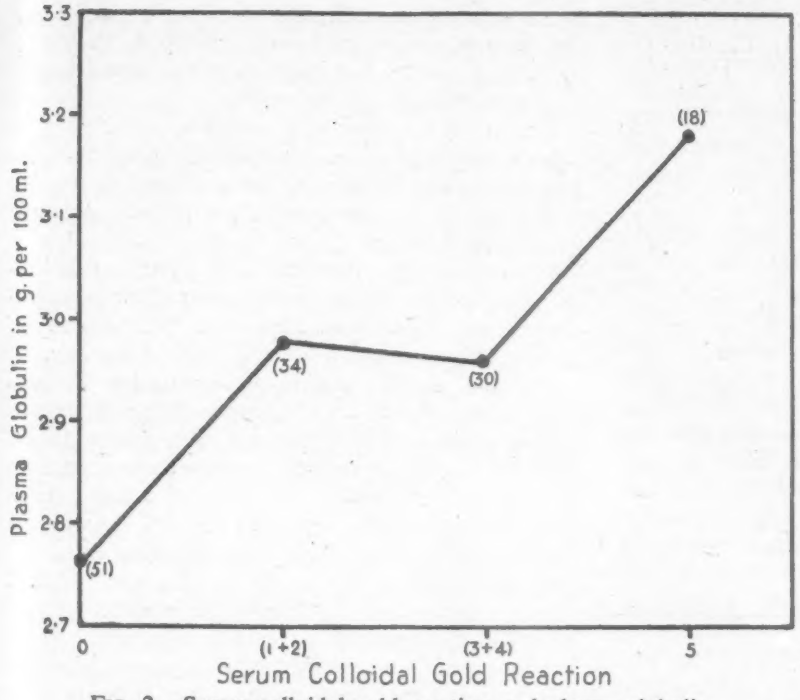

FIG. 2.—Serum colloidal gold reaction and plasma globulin (number of observations shown in brackets).

proteins and the various protein fractions. While the results of the serum colloidal gold reaction did not show any apparent relation to the total protein and fibrinogen, there was a moderate degree of relationship with the albumin and globulin fractions, inverse in the former and direct in the latter (Figs. 1 and 2). The method of charting the results was as follows: the serum colloidal gold values were arranged and recorded in four groups only—viz., 0, 1+ and 2+, 3+ and 4+, 5+,—for this reason; while the results of the serum colloidal gold reaction are generally recorded in one of six groups, 0, 1 +, 2+, 3+, 4+, and 5+, considerable difficulty arose in many cases in distinguishing between a 1+ and a 2+ reading, and between a 3+ and a 4+, as the difference in the amount of flocculation between these figures is small. The corresponding values of the protein fractions in the four groups were averaged.

The results of the cephalin-cholesterol flocculation test did not show any relationship to the plasma proteins.

Other factors.—An attempt was made to correlate the results of the serum colloidal gold and cephalin-cholesterol flocculation tests with various clinical findings. No relationship was found between either of the tests and the age, sex, duration and degree of arthritis, weight, temperature, white cell count, haemoglobin, focal sepsis, or previous gold therapy.

Other Forms of Rheumatism.—As an additional control series it was considered advisable to perform the serum colloidal gold and cephalin-cholesterol flocculation tests on patients with other forms of rheumatism. Observations were made on thirty patients with osteo-arthritis, twenty with rheumatic fever, twenty with fibrositis, and two with ankylosing spondylitis. The results are shown in Table 3.

It will be seen from the Table that in osteo-arthritis and fibrositis the results of both tests were uniformly negative. One of the two patients with ankylosing spondylitis gave a mildly positive reaction (1+) with the serum colloidal gold test, while the cephalin-cholesterol flocculation test was negative in both. In rheumatic fever, eight (40 per cent.) of the twenty patients had positive reactions with the serum colloidal gold test, and three (15 per cent.) with the cephalin-cholesterol flocculation test. The results are shown in greater detail in Table 4.

TABLE 3

SERUM COLLOIDAL GOLD AND CEPHALIN-CHOLESTEROL FLOCCULATION TESTS IN OTHER FORMS OF RHEUMATISM

	No. of cases	Colloidal gold		Ceph. chol.	
		Pos.	Neg.	Pos.	Neg.
Osteo-arthritis ..	30	0	30	0	30
Rheumatic fever ..	20	8	12	3	17
Fibrositis	20	0	20	0	20
Ankylosing spondylitis	2	1	1	0	2

Effect of Gold Therapy.—The serum colloidal gold and cephalin-cholesterol flocculation tests were performed on thirty patients with rheumatoid arthritis before and after receiving one course of myocrisin injections (total=1 g.).

Clinically, twenty-five of the thirty patients responded favourably to the gold therapy, the remainder showing no change in their condition. While the results of the serum colloidal gold reaction

TABLE 4

SERUM COLLOIDAL GOLD AND CEPHALIN-CHOLESTEROL FLOCCULATION TESTS IN RHEUMATIC FEVER

Cephalin-cholesterol	Colloidal gold						Totals
	0	1+	2+	3+	4+	5+	
0	12	0	1	2	2	0	17
+	0	0	0	0	0	0	0
++	0	0	1	0	0	0	1
+++	0	0	0	0	1	0	1
++++	0	0	0	1	0	0	1
Totals ..	12	0	2	3	3	0	20

TABLE 5

CEPHALIN - CHOLESTEROL FLOCCULATION TEST BEFORE AND AFTER GOLD THERAPY IN THIRTY CASES OF RHEUMATOID ARTHRITIS

		Cephalin-cholesterol					
		0	+	++	+++	++++	Totals
No. of cases	Before	19	2	2	4	3	30
	After	29	1	0	0	0	30

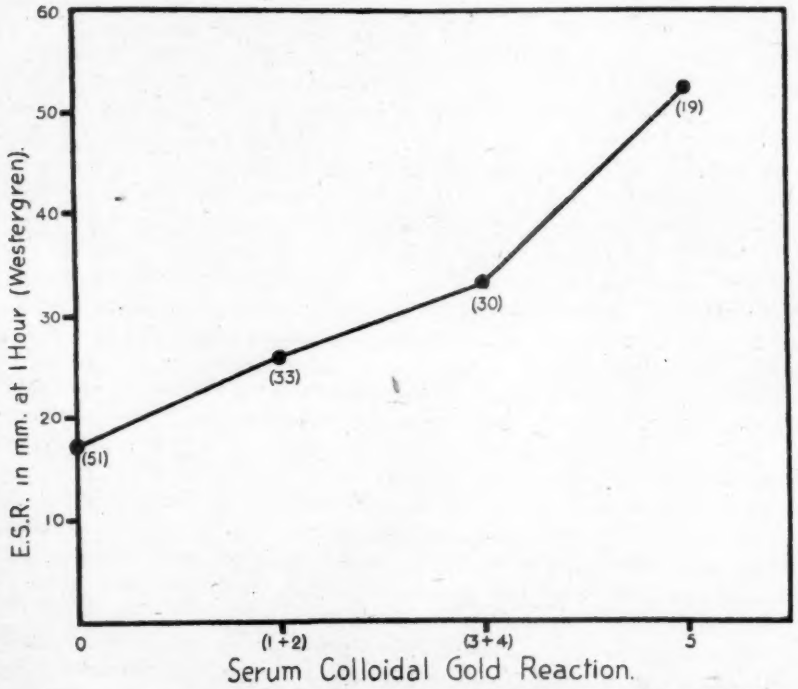

FIG. 3.—Serum colloidal gold reaction and erythrocyte sedimentation rate (number of observations shown in brackets).

as a whole showed a change towards normal following therapy, the amount of improvement shown by the test, however, was only partially related to the degree of clinical improvement.

Eleven of the thirty patients who received gold therapy had a positive cephalin-cholesterol flocculation test before treatment. It is of interest to note that in ten of the eleven cases the test was negative at the end of therapy (Table 5).

It was found that there was only a partial relationship between the change in the results of the cephalin-cholesterol flocculation test and the degree of clinical improvement following on gold therapy.

Relation to Erythrocyte Sedimentation Rate.—It was considered of interest to see whether the results of the serum colloidal gold test were related to the changes in the erythrocyte sedimentation rate in rheumatoid arthritis. The results have been recorded graphically in Fig. 3. As before, the colloidal gold values have been arranged into four groups as follows: 0, 1+ and 2+, 3+ and 4+, 5+. The corresponding erythrocyte sedimentation rate values in these groups have been averaged. There would appear to be a moderate degree of relationship between the results of the serum colloidal gold reaction and the erythrocyte sedimentation rate.

As the cephalin-cholesterol flocculation test was positive in only 19 per cent. of the estimations the findings have not been recorded graphically, as it was felt that to do so would give an erroneous picture.

Discussion

Although the flocculation tests are now being employed as a routine in many hospitals, there is still no satisfactory explanation of their mechanism. While in hepatic disease there is some relation between the positive results and the degree of destruction of liver tissue, there is no evidence to suggest that the high percentage of positive findings with the serum colloidal gold test in rheumatoid arthritis is in any way related to liver damage. Baggenstoss and Rosenberg (1943) studied at necropsy the pathological changes in the viscera in thirty patients with rheumatoid arthritis and failed to observe any characteristic hepatic lesion which could be ascribed to

the disease. It is possible, as Enders (1944) has shown in other diseases, that an antibody attached to the serum gamma-globulin fraction may account for the flocculating power of the blood of patients with rheumatoid arthritis.

In the present investigation an attempt was made to see whether the results of the serum colloidal gold reaction were in any way related to alterations in the plasma proteins. It was found that, whereas there was no apparent relation to the total protein and fibrinogen, there was a moderate degree of relationship with the albumin and globulin fractions, inverse in the former and direct in the latter. It may be, therefore, that a positive serum colloidal gold reaction in rheumatoid arthritis depends on both a quantitative, as well as a qualitative, change in certain of the plasma protein fractions.

It has been shown that in patients who responded favourably to gold therapy the degree of clinical improvement was not accurately reflected by the results of the serum colloidal gold test. For instance, those patients who had shown the greatest clinical improvement would have been expected to have had negative or only mildly positive serum colloidal gold reactions, but this was not invariably the case. This may, of course, be due to the fact that the test takes longer to return to normal than clinical recovery.

A comparison between the results of the serum colloidal gold reaction and the erythrocyte sedimentation rate in rheumatoid arthritis showed that there was a definite relationship between the two tests—for example, there were thirty observations with normal sedimentation rates (up to 10 mm.), the corresponding serum colloidal gold test being negative in all but seven instances, and in these only a mild positive reaction was obtained (1+).

The serum colloidal gold test is thus of value in rheumatoid arthritis, although, as with the erythrocyte sedimentation rate, too much reliance should not be placed on it. As an indicator of the activity and as a guide to the progress of the disease it is probably a less sensitive test than the latter. It is useful, too, in the differential diagnosis between rheumatoid arthritis on the one hand and osteo-arthritis and fibrositis on the other. Unfortunately, it is not of any value in the differentiation of rheumatoid arthritis from rheumatic fever, as the test is also positive in an appreciable number of cases of the latter disease. It may be that some factor common to both rheumatoid arthritis and rheumatic fever is responsible for this finding.

There is little to commend the use of the cephalin-cholesterol flocculation test in rheumatoid arthritis, as it was positive in only one-fifth of the observations.

Summary

1. The serum colloidal gold test was positive in 61 per cent. of the observations in rheumatoid arthritis and in 40 per cent. of the cases of rheumatic fever. In osteo-arthritis, fibrositis, and normal controls the results were uniformly negative.

2. The cephalin-cholesterol flocculation test gave a positive reaction in 19 per cent. of the observations in rheumatoid arthritis and in 15 per cent. of the cases of rheumatic fever. Negative results were obtained in all the cases of osteo-arthritis, fibrositis, and ankylosing spondylitis, and in all the normal controls.

3. There was a moderate degree of relationship between the results of the serum colloidal gold reaction and the plasma albumin and globulin fractions, inverse in the former and direct in the latter. There was no apparent relation to the total protein or fibrinogen fraction.

4. A relationship was observed between the results of the serum colloidal gold test and the erythrocyte sedimentation rate. It is concluded that the former is a useful test in rheumatoid arthritis, although a little less sensitive than the latter.

5. The cephalin-cholesterol flocculation test would appear to be of little value in rheumatoid arthritis.

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Epreuves de Floculation dans l'Arthrite Rhumatismale

RÉSUMÉ

Cette étude a été entreprise dans le but de déterminer si l'une des épreuves de floculation, et particulièrement la réaction à l'or colloïdal, peuvent présenter un intérêt, non pas comme une épreuve diagnostique comme dans les maladies du foie, mais pour fournir une indication

de l'activité ou servir de guide dans le prognostic de l'arthrite rhumatismale. Les résultats ont été les suivants:

1. L'épreuve à l'or colloïdal a été positive dans 61 pour cent des cas d'arthrite rhumatismale, et dans 40 pour cent des cas de rhumatisme articulaire aigu. Dans l'ostéo-arthrite, dans la cellulite, et chez les sujets normaux, les résultats ont été uniformément négatifs.

2. L'épreuve de floculation céphaline-cholestérol a donné une réaction positive dans 19 pour cent des cas d'arthrite rhumatismale et dans 15 pour cent des cas de rhumatisme articulaire aigu. On a eu des résultats négatifs dans tous les cas d'ostéo-arthrite, de cellulite, de spondylite ankylosante, et chez tous les sujets normaux.

3. Il existe un certain degré de corrélation entre les résultats de la réaction à l'or colloïdal et les fractions albumine et globuline du plasma, inverse pour la première et directe pour la seconde. Il n'y avait pas de relation apparente avec la protéine totale ou la fraction fibrinogène.

4. On a observé une relation entre les résultats de l'épreuve à l'or colloïdal et le taux de sédimentation sanguine. On en a conclu que la première est une épreuve utile dans l'arthrite rhumatismale, mais moins sensible que la seconde.

5. L'épreuve de floculation céphaline-cholestérol semble n'avoir que peu de valeur dans l'arthrite rhumatismale.

INTERSTITIAL NEURITIS AND THE NEURAL THEORY OF FIBROSITIS*

BY

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Interstitial neuritis, or fibrositis of the sheath of a nerve trunk, is characterized by five chief signs or symptoms (Harris, 1926; Walshe, 1943): (1) radiating pain; (2) tenderness in the vicinity of a nerve trunk; (3) paraesthesiae or objective sensory loss; (4) muscular wasting or paresis; (5) loss of deep reflexes.

If the distribution of the pain and tenderness, however, is such as to suggest the involvement of a nerve trunk, the diagnosis may be made in the absence of the remaining three criteria. Motor and sensory signs are encountered in only a minority of cases (Walshe).

The Pathology of Interstitial Neuritis

"Of the pathological process which underlies this familiar affection," wrote Walshe, "relatively little is known, but it involves the interstitial tissues of the nerve roots and trunks and not, save secondarily in some cases, the nervous elements." Symonds (1943) contends that its pathology is built upon guesswork, for the neurologist rarely sees the nerve which is supposed to be affected. Purdon Martin (1933) thought that the pain of neuritis could not be produced solely by pressure upon axis cylinders; he suggested that it must be related to an altered state of the nervi nervorum. The orthodox view holds that the rheumatic inflammation of the sheath, with its consequent swelling, interrupts the neuraxons by mechanical pressure. It is not necessary, however, to postulate such a mechanical element, for the rheumatic agent is well known to be capable of bringing about the death or degeneration of specialized tissues. If we agree that the fibrositic process may attack the fibrous sheath of a nerve, it follows that the nerve fibres may be poisoned by the diffusion of the rheumatic agent. Bentley and Schlapp (1943) demonstrated that the pressure necessary to interrupt conduction in a nerve trunk is very much greater than any that could develop in an inflammatory swelling; and here we have no proof that there is even any swelling.

Taking the five criteria in order, it will be seen that interstitial neuritis often is not easy to differentiate from fibrositis.

Radiating Pain.—Pain from deep somatic lesions radiates in a characteristic fashion. Thus, pain from a lesion in the shoulder-girdle may radiate to the elbow and even to the fingers. In spite of what is commonly believed, too, pain is not a characteristic feature of pressure on nerve trunks (Head and Sherren, 1905). The observer can verify this in a short time by compressing his own ulnar nerve at the elbow. Local tenderness can be elicited, of the same order as that of a musculo-tendinous junction; while the sensation which radiates to the hand is not pain, but tingling and warmth. The fact that a "neuritic" pain radiates, therefore, does not necessarily signify the presence of a lesion of a nerve trunk.

Deep Tenderness.—The diagnosis of neuritis is confirmed by the presence of tenderness of the nerve trunk, limited to it. But most nerves are not directly palpable; when diffuse tenderness occurs in the region of a nerve trunk, it should be remembered that the nerve lies deep to structures which themselves are tender. This tenderness, moreover, may be of a secondary nature, disappearing upon anaesthetization of a somatic lesion which bears no relation to the nerve trunk. Such a result has been secured with procaine in a number of cases which fulfilled the first two criteria of interstitial neuritis; in none of them did injection of the lesion cause blocking of the nerve (Kelly, 1945, 1946*a* and *b*). Tenderness in the region of a nerve trunk, said Harman (1940) is not necessarily due to primary inflammation of the nerve, for equally tender spots can be demonstrated far from the nerve.

Paraesthesiae or Objective Sensory Loss.—Tingling in the extremities, or other abnormal sensations, may result from deep lesions (Kellgren, 1938, 1939). Hyperalgesia of the skin is not pathognomonic of a nerve lesion, for it appears as an occasional reflex effect of a deep somatic lesion. Anaesthesia or

* This paper is part of the Buckston Browne Prize Essay for 1946, the title of the essay being "The Pathology and Treatment of Fibrositis".

hypo-aesthesia, however, usually is regarded as presumptive evidence of interruption of nerve-conduction.

Muscular Wasting and Paresis.—Muscular wasting alone is not evidence of a trunk lesion, for reflex wasting occurs in disease of joints, and sometimes rapid wasting follows mild trauma to a muscle (Case 10). Paresis of a muscle, however, is evidence of mechanical interference with neuraxons.

Loss or diminution of deep reflexes is generally held to be pathognomonic of a nerve lesion. The work of Gellhorn and Thompson (1944), however, suggests that these effects may result also from local abnormalities of muscle (*vide infra*).

Differences between Neuritis and Traumatic Nerve Lesions

Interstitial neuritis, therefore, should not be diagnosed unless muscular paresis or objective sensory loss is evident. The criteria which distinguish fibrositis of a nerve sheath from intramuscular fibrositis are those of a nerve lesion, and a nerve lesion should not be diagnosed when they are absent. If there is a localized lesion affecting the nerve trunk, the signs should closely resemble those of a traumatic "lesion in continuity", in which injury has caused interruption of conduction without severing the nerve. While this close resemblance does exist in many cases, in some others the general picture of fully developed neuritis differs in four important details from that of injury to a nerve trunk: (1) pain; (2) delayed onset; (3) anatomical distribution of manifestations; (4) amount of final recovery.

Pain.—While severe pain is a characteristic feature of neuritis, it is not so in nerve injury. In only three out of twenty-four cases of "neurapraxia" reported by Seddon (1943) was pain prominent. Pain was not a feature of the cases of injury to the brachial plexus which Clausen (1942) reported, while all of Richardson's series (1942) of "winged scapulae" of non-traumatic origin were accompanied by severe pain. Pain is an added feature of neuritis, to be expected because fibrositis is a painful disorder, whether or no a nerve-sheath is involved.

Delayed Onset.—When a nerve is involved in an injury, the evidence of paralysis usually comes on rapidly. In many cases neuritis follows injury or other damage to tissues; but the onset usually is delayed for some days, and often for some weeks (see Cases 2, 6, 7, 9, 11, 12). This usually is explained as the time during which the process has been spreading to involve the nerve sheath.

Anatomical Distribution of Manifestations.—When a nerve has been injured, the motor and sensory signs usually are related only to the field of the nerve. When, on the other hand, similar effects result from neuritis, they often overflow into the fields of other nerves. In Case 1, for example, a lesion of the circumflex nerve had overflowed to affect branches of the posterior cord of the brachial plexus.

CASE 1.—A Private, after a sore throat, suffered from pain in the right shoulder, with weakness of abduction. Seven weeks later he presented: (a) profound wasting of the deltoid, with minimal voluntary contraction; (b) diffuse deep tenderness over the acromion and the upper part of the deltoid; diminution of cutaneous sensibility in the areas supplied by the circumflex nerve and the digital branches of the radial nerve.

A year later there was no residual wasting, though he complained of weakness and aching pain.

In Case 2 a posterior cord lesion could not be diagnosed because of the damage to the suprascapular nerve, which is a branch of the upper trunk. The disorder can be explained only as a lesion of several roots.

CASE 2.—A Warrant Officer injured his right shoulder, and for some weeks suffered from a pain which radiated from the shoulder to his right ear. Later it was replaced by a pain in the left shoulder, which radiated to the wrist. The muscles of the left forearm were weak. Three months after the original injury he presented no sensory loss; but all the muscles supplied by the dorsal interosseous nerve were paretic and grossly wasted. In addition, the left deltoid and infraspinatus had undergone gross atrophy.

Similar cases of neuritis of the brachial plexus have been reported in British and Dominion Armies (Burnard and Fox, 1942; Richardson, 1942; Spillane, 1943). Bilateral lesions were reported in seven of Spillane's forty-seven cases, and in two of Richardson's nine. In Case 3, bilateral lesions of unknown origin were seen.

CASE 3.—A Private complained of pain in his left shoulder, which shifted to the right after two weeks, with limitation of abduction of the right humerus. Six weeks from the commencement he presented: (a) "winging" of the right scapula, with weakness of abduction; (b) profound wasting of the left spinati.

In some cases large patches of anaesthesia may be seen, with no relation to any radicular or peripheral nerve distribution. These cases often are labelled hysteria because they cannot be explained upon anatomical grounds.

CASE 4.—This was a case of musculo-cutaneous neuritis with widespread hypo-aesthesia. A Private had numbness and weakness of the right arm which came on without apparent cause. The forearm felt numb, and flexion of the elbow was feeble. There was no voluntary contraction in the biceps; but the brachialis retained slight contractility. Cutaneous pain and touch were diminished or absent below a line running obliquely from two inches below the lateral epicondyle to two

inches above the medial. The degree of loss varied in a patchy manner, and sensation was normal on the palmar surfaces of the digits. Complete recovery occurred in two months.

The Amount of Final Recovery.—After a traumatic "lesion in continuity", in which the neural pattern is not disturbed, recovery usually is complete. Seddon reported poor results in only thirteen out of 230 such lesions; while Sunderland (1945) found that the final outlook was good in a series of cases of pressure-palsy of the radial nerve.

In interstitial neuritis, on the other hand, the results are worse; thus Bennett (1939) found that 20 per cent. of 115 cases of "horse serum neuritis" were left with residual disabilities; the results reported by Burnard and Fox and by Spillane were not any better. Of the present series of 63 cases of interstitial neuritis, at least seventeen had not recovered fully within periods varying from one to three years. Such a lesion as occurs in neuritis must of a certainty be a "lesion in continuity"; yet exploration of the nerve never has revealed a macroscopic lesion, and the few microscopic examinations which have been performed have given negative results. Neuraxons possess almost irrepressible powers of regeneration so long as they retain functional connexion with the parent cells. The picture of interstitial neuritis which has failed to recover, therefore, is not consistent with the supposition that a localized lesion of a nerve has occurred. The wasting sometimes is so profound and so enduring that one is reminded of the sequelae of poliomyelitis.

The Causation of Interstitial Neuritis

The causes of interstitial neuritis are the same as those of fibrositis in general. It may occur as a manifestation of generalized rheumatism, or it may come on without apparent cause. Of the present series of sixty-three cases, in forty-six the onset could be related clearly to a causative factor. In thirty-three the cause was local, while in the remaining thirteen the neuritis followed systemic disease, or trauma to a distant region. Of the local causes, trauma, muscle strain, or infection were the agent in twenty-four, synovitis or osteo-arthritis of a neighbouring joint in five, herpes zoster in three, and subcutaneous lipomata in one. Of Spillane's forty-seven cases of brachial neuritis, twenty-seven occurred in patients already under treatment in hospital for other disorders, such as systemic infections and septic wounds. Local causes seem more significant where only one nerve is involved, as in five cases reported by Nielsen (1939), in which paralysis followed a single muscular effort. Ecker and Woltman (1938) were able to find local causes in sixty-one out of 150 cases of "meralgia paraesthetica."

Local injury, or other damage to tissues, thus plays a large part in the causation of interstitial neuritis. In most of those which followed injury, the nerve could not have been involved in the primary damage. In sixteen cases the manifestations which followed local injury or disease had spread more widely, so that they could not be explained upon the basis of simple lesions of nerve trunks. In several cases (of which Case 11 is an example), it was possible, by the use of local analgesia, to relieve temporarily or to cure the pain, without intensifying the partial block of the nerve. Seldom, indeed, was the deep tenderness of the myalgic lesion in the vicinity of any nerve trunk.

The Reflex Theory Applied to the Manifestations of Neuritis

The signs and symptoms of interstitial neuritis have been listed under five headings. Of these the first two, (1) radiating pain, and (2) deep tenderness, are reflex effects, for the injection of procaine into a myalgic lesion brings about their immediate disappearance. Sensory and motor disturbances, however, must be regarded as presumptive evidence of a nerve lesion. But in some of these cases the signs would spread far beyond the field of the trunk which seemed to be implicated. In these the older writers used to suppose the existence of an "ascending neuritis", whose pathology was obscure. It is certain, at any rate, that the orthodox conception of neuritis is not sufficient to explain the spreading nature of the manifestations. It is opportune now to inquire if they can be accounted for adequately by the reflex hypothesis recently suggested for fibrositis (Kelly, 1945, 1946*a* and *b*).

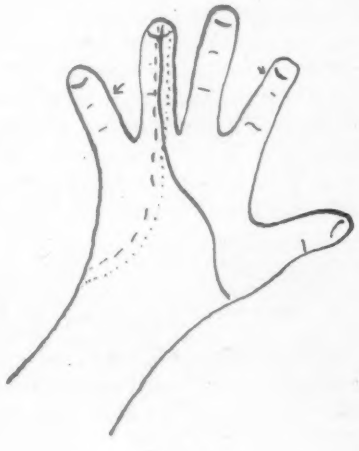

FIG. 1.

Abnormal Cutaneous Sensation.—The late Sir Thomas Lewis (1942) observed that faradization of a digital nerve resulted in hyperalgesia through the distribution of the main cutaneous nerve (Fig. 1). Again, antidromic stimulation of a sensory trunk gave rise to hyperalgesia throughout its distribution. A good deal of converging evidence suggests that these effects are brought about through the medium of the pain nerves and their receptors. Similarly, cutaneous hyperalgesia sometimes resulted from artificial deep lesions; this Lewis regarded as a reflex effect, the nervous impulses overflowing from the deep into the cutaneous system. Though this work has rendered familiar the idea of the reflex production of hyperalgesia, the concept of reflex production of anaesthesia might seem far-fetched. But Thompson (1931) reported some years ago that faradization (through the skin) of a cutaneous nerve resulted in anaesthesia in its distribution; he made use of this method in outlining the areas of distribution of sensory nerves. At the same time Adrian and others (1931) reported experiments which suggested that the mechanical stimulation of touch receptors in the frog's skin resulted, through reflex action, in the diminution of activity in adjacent receptors. All of these observations are consistent with the supposition that abnormalities of cutaneous sensation may be a reflex effect of the activities of somatic tissues. The observations of Thompson are not inconsistent with those of Lewis, for it is a recognized neurological principle that hyperalgesia and anaesthesia may represent two different stages of the same pathological process (Kinnier Wilson, 1927).

In the condition called Sudeck's atrophy or post-traumatic painful osteoporosis, large patches of cutaneous anaesthesia may be found which do not correspond with the distribution of any nerve (Livingston, 1943; Miller and De Takats, 1942). These were regarded as the effects of reflex impulses. Sometimes a patch of anaesthesia was confined to the field of a cutaneous nerve; this Miller and De Takats regarded as evidence of involvement of the nerve trunk in the original injury. Having admitted the hypothesis of reflex anaesthesia, however, it would seem permissible to regard these also as reflex effects, confined more accurately to the distribution of a single nerve.

CASE 5.—This was a case of reflex anaesthesia following sprain of the external lateral ligament of the knee joint. A driver injured his right knee in a derailment accident. The joint was stiff and painful a month later, with nocturnal aching and much limitation of movement. The pain was felt on the outer side of the knee, and the skin all around the joint felt numb. On examination the joint was not swollen. Only 15° of flexion was possible. The outer aspect of the joint-line was extremely tender to pressure. Cutaneous sensations of touch and pain were almost completely abolished over an area surrounding the limb and extending both above and below the joint-line for a distance of four inches (Fig. 2).

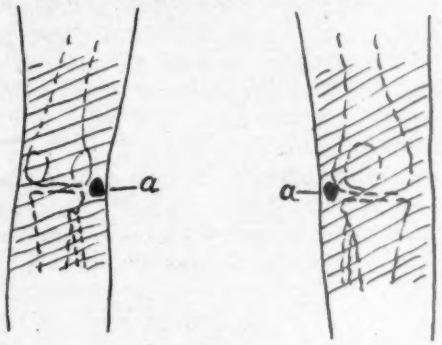

FIG. 2.

CASE 6.—This case showed anaesthesia in the distribution of the lateral cutaneous nerve of the thigh, following injury to the knee. A soldier sprained his right knee, which became distended with fluid. It was slow to recover, and after two months he complained of numbness of the thigh. Examination revealed: (1) a knee joint distended with fluid; (2) gross wasting of the quadriceps femoris; (3) anaesthesia in the distribution of the lateral cutaneous nerve. The skin was smooth and atrophic (Fig. 3).

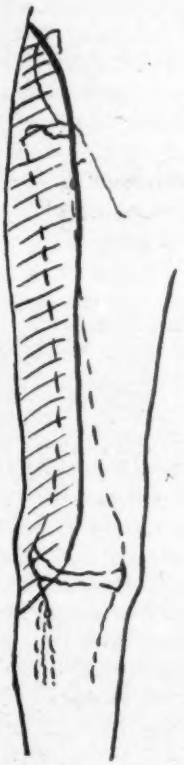

FIG. 3.

CASE 7.—This was a case of neuritis of the lateral cutaneous nerve of the thigh, the reflex effect of multiple lipomata. A young soldier complained that for 2 years he had had painful lumps on his abdomen and right thigh. The skin over each lump on the abdomen was itchy, and the thigh had a " pins-and-needles " feeling over a larger area, with an aching pain which was made worse by weight-bearing. Examination revealed : (1) on the abdomen: four subcutaneous lipomata, each of which was surrounded by an area of cutaneous hyperalgesia; (2) on the right thigh seven lipomata more closely grouped, with an area of hyperalgesia occupying the outer surface of the thigh, and extending from the iliac crest to the level of the knee joint (Fig. 4).

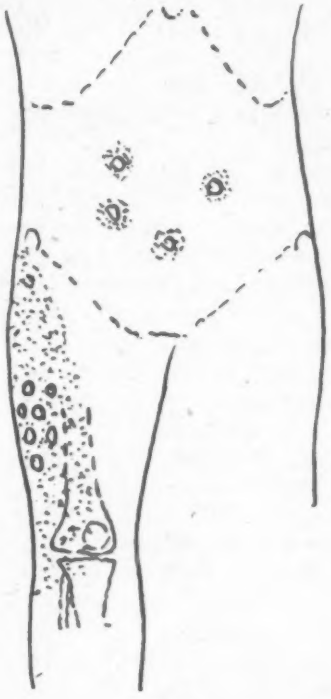

FIG. 4.

Case 7 provides strong support for the reflex theory of neuritis. The small patch of hyperalgesia around each isolated lipoma must have been a reflex effect from the tumour. On the thigh, where the lumps were more numerous and grouped more closely, the areas of hyperalgesia had enlarged and coalesced, and spread to involve the whole distribution of a large cutaneous nerve.

CASE 8.—This case had ulnar anaesthesia after mild crushing injury to the hand. A seaman suffered a slight crushing injury to the hand in February, 1942. Since then it had been painful, with an ache ascending along the inner side of the forearm. Late in June he complained of severe pain and of numbness in the hand and lower part of the forearm. On examination seven months after the injury, anaesthesia was found in the distribution of the ulnar nerve in the hand, spreading upwards for six inches along the ulnar side of the forearm. A point of acute tenderness was found in the fourth interosseous space (Fig. 5).

FIG. 5.

CASE 9.—This case had a partial lesion of the dorsal cutaneous nerve of the forearm after fracture of the lower end of the radius. A Sergeant fractured the lower end of his radius. Plaster was applied, and removed seven weeks later. For two months after this the wrist remained stiff, with a tendency to swell on the dorsum. He complained of an ache at night, with pain shooting along the dorsum of the forearm. On examination there was found to be cutaneous hyperalgesia of the distal half of the dorsum of the forearm. Movements of the wrist were limited by a painful stiffness, though the fracture had united normally. The pain in the forearm was completely abolished by injecting with procaine a tender spot in the extensor mass near the musculo-tendinous junction.

A number of like cases could be cited, and all indicate that reflex sensory effects may approximate to the distribution of a cutaneous nerve. In other cases they are more diffuse, resulting in anaesthesia of a more irregular distribution (as in Cases 4 and 5).

Paralysis and Wasting of Muscles.—These are signs of interference with the lower motor neurone. In interstitial neuritis, complete paralysis is encountered only occasionally, and wasting may be absent. In the profound wasting which sometimes

accompanies joint disease, groups of muscles are involved which are functionally connected with the joint, and reflex activity may be increased. "It is not a mere wasting from disuse," said Sir James Paget (1879), "it is far more rapid than that; . . . I wish I could explain it better than by calling it reflex atrophy . . . due to the disturbance of some nutritive nerve centre, irritated by the painful state of the sensitive nerve fibres." In experiments on rabbits, Harding (1929) was able to show that this reflex wasting depended upon the integrity of the afferent nerves from the limb.

CASE 10.—This case showed wasting of the biceps muscle after contusion. A Sergeant received a blow on the front of the humerus just below the shoulder joint. For two months afterwards he complained of pain in this region, with weakness of the shoulder. Examination revealed: (1) gross wasting of the biceps muscle; (2) a well-defined tender spot in its upper fibres, near the musculo-tendinous junction. Infiltration abolished the pain permanently, but many weeks elapsed before the atrophy had recovered.

Reflex wasting is not paralysis; but sometimes an injury is followed by a paresis of a group of muscles supplied by a nerve which could not have been involved in the injury.

CASE 11.—This case was one of dorsal interosseous paresis after a blow on the wrist. A Private knocked his left wrist, and next day it ached. The pain spread to the elbow, and four days later he "reported sick" with numbness in the fingers and loss of power in the hand. No cutaneous sensory loss could be found; but only the slightest flicker of contractility was present in the extensor group of muscles, and flexion of the fingers also was much weakened.

Five weeks later the pain was continuous, though some movement was returning to the muscles. A tender spot was found in the common site three inches below the lateral epicondyle. An injection of procaine relieved the pain without completing the block of the dorsal interosseous nerve. The pain did not return, and he made a good recovery within a few weeks.

CASE 12.—In this case there was suprascapular nerve paralysis after a bullet wound in the region of the lower angle of the scapula. A Private was shot through the left side of the chest in October, 1943. He made a good recovery; but a month later an aching pain commenced behind the shoulder which persisted for a year. Examination ten months after his injury revealed: (1) a healed wound of entry just medial to the inferior angle of the scapula; the bullet itself was resting just behind the 8th costal cartilage; (2) limitation of active abduction to 60°, though there were no adhesions in the scapulo-humeral joint; (3) profound wasting of the spinati; there was no evidence that any fibres of the infraspinatus had survived.

Electromyography.—A denervated muscle displays abnormal activity in the shape of fibrillation. Sometimes this phenomenon can be observed with the eye, but as a rule it can be detected only by electromyography. Weddell and others (1944) have observed that the wasted muscles of interstitial neuritis and "radiculitis" give varying responses, depending upon whether or no denervation has been complete. Disordered and increased muscular activity was recorded as a routine from the areas of maximum muscular tenderness in neuritis and fibrositis. This observation was confirmed by Elliott (1944), who recorded also abnormal activity in muscles which were the site of transient tenderness "referred" from an artificial deep lesion.

Muscular wasting, weakness and fibrillation, therefore, all represent disorders of muscular function which can be brought on by somatic agencies through reflex channels.

Deep Reflexes.—An absent ankle-jerk is regarded by many as a criterion of organic interference with nerve tracts; and the same may be said of the diminution of deep reflexes in general. The experiments of Gellhorn and Thompson (1944), however, suggest that reflexes may be abolished as the result of abnormal conditions within the muscle. By causing the triceps muscle to work under ischaemic conditions, continuous aching pain was produced in ten subjects whose triceps reflexes had been particularly brisk. With the onset of the pain, the deep reflex was abolished, to reappear soon after the restoration of the blood flow. There is a close analogy between ischaemic pain and fibrositic pain, and it should not be surprising occasionally to find that the loss of deep reflexes is merely the effect of a deep somatic lesion. Wartenberg (1944) has deprecated the habit of regarding the absence of a single deep reflex as a sign of central nervous disease; the evidence provided by the reflexes, he said, should be weighed only in conjunction with other neurological signs.

Reflex Paralyses

The interpretation of the spreading paralyses has undergone a number of fluctuations. Weir Mitchell (1872) had no doubt that the manifestations had a physical basis, and he called them reflex paralyses. He suggested, too, that the nerve impulses which bring about the manifestations must run in a direction opposite to the normal. Babinski and Froment (1918) described a large number of cases in wounded French soldiers. They were emphatic that the disorder bore none of the criteria of hysteria, and their reasons today seem convincing. They coined a new word, "physiopathic", for these disorders, indicating that, though the underlying pathology

was not understood, they had no doubt of its organic nature. They did not subscribe to the commonly accepted view, epitomized in the term "ascending neuritis", which supposed that a toxin from the infected wounds had entered the peripheral nerve filaments and ascended the neuraxon. Walshe (1919), citing a case of sciatic palsy which followed a blow on the heel, observed that infection did not always precede the paralysis. But the late Sir Arthur Hurst (1919) regarded every such case as hysterical, and his view came to prevail. About the majority of these patients there is little that suggests the hysteric; but it is a melancholy fact that many of them do acquire this damaging stigma. Orthodox clinical neurology is based upon rigid anatomical data, and disorders which do not correspond often receive but scant consideration. We should not be surprised, therefore, to find that recent studies upon the organization of the spinal cord and upon the functions of the peripheral nerves suggest the possibility that such a physical basis does exist.

The Sensory Organization of the Cord

Is the reflex hypothesis of fibrositis (and of interstitial neuritis) consistent with present knowledge of the physiology of the spinal cord? Do pathways exist through which the supposed disordered impulses must travel? The motor organization of the cord, we know, has as its basis movements rather than individual muscles or individual segments of the cord (Sherrington, 1906). A simple reflex movement requires a complicated form of co-ordination which spreads over a large number of segments, bringing about the stimulation of some groups of muscles and the inhibition of others. It is possible that sensory impulses may be subject to an analogous form of co-ordinated spread; indeed the large number of collaterals which proceed from sensory radicles would seem to imply some sort of interlinking of sensory neurons. And recent neurophysiological work seems to indicate that such a sensory reflex organization exists. In addition to the sensory impulses which ascend directly to the cerebrum, delayed discharges of a reflex nature can be recorded which spread upwards in the cord and outwards through the posterior roots (Toennies, 1938; Barron, 1940; Hursh, 1940). "The nervous system", wrote Lorente de Nó (1938), "is composed of an exceedingly large number of interlacing pathways which offer numerous opportunities for the conduction of impulses into divergent paths; but during activity it becomes fractionated into a group of active and a group of inactive neurones." The integrating mechanisms, in other words, ensure that stimulation and inhibition proceed side by side, in both the motor and the sensory provinces, without becoming deranged. Lorente de Nó used the term "internuncial pool" to describe the neuronal systems through which the impulses are relayed, and the idea was further developed by Livingston in his excellent monograph (1943). Livingston argues convincingly in favour of the reflex hypothesis; it seems that a succession of abnormal sensory impulses (such as may proceed from diseased or damaged tissue), continued over a long period, may permanently damage the integrating mechanism, resulting in a state of imbalance. Thus, if normal stimuli cause certain neurones to be activated and others to be inhibited, prolonged abnormal stimulation may result in intensification and prolongation of the stimulation on the one hand, and of the inhibition on the other. These changes would manifest themselves as intractable motor and sensory abnormalities.

Summary

1. The pathology of interstitial neuritis remains in a state of obscurity.

2. Radiating pain and perineural tenderness do not constitute sufficient evidence on which to make this diagnosis, for they often represent the secondary effects of a myalgic lesion.

3. The diagnosis should be made only if there is motor or sensory loss to indicate interference with nerve conduction; and even these cases sometimes differ in a striking fashion from proven "lesions in continuity".

4. In thirty-three out of sixty-three cases, the onset of interstitial neuritis could be related to local injury or disease. In most of these it was not likely that the damage could have involved the nerve trunk directly.

5. In some cases the sensory and motor manifestations were observed to spread beyond the fields of any nerves which could have been implicated.

6. These anomalous features are explained in the light of a reflex hypothesis previously proposed for fibrositis.

7. It is an error to diagnose hysteria in these cases. Reference is made to the views of Babinski on reflex paralysis, and to those of Lorente de Nó on the sensory organization of the cord.

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Névrite Interstitielle et Théorie Nerveuse de la Cellulite

RÉSUMÉ

1. La pathologie de la névrite interstitielle reste obscure.

2. La douleur irradiante et la sensibilité périneurale ne constituent pas une preuve suffisante permettant d'établir un diagnostic car elles constituent souvent les effets secondaires d'une lésion musculaire.

3. On ne doit faire ce diagnostic que lorsqu'il existe une déficience motrice ou sensorielle indicatrice d'un trouble de la conduction nerveuse ; et il arrive même que certains de ces cas diffèrent de façon marquée des " lésions en continuité " démontrées.

4. Dans 33 cas sur 63, on a pu établir une corrélation entre le début de la névrite interstitielle et un traumatisme ou une maladie localisés. Dans la plupart de ces cas il était peu probable que la lésion ait atteint directement le tronc nerveux.

5. Dans certains cas on a observé que les manifestations sensorielles et motrices s'étendaient au-delà du territoire des nerfs qui auraient pu être atteints.

6. Ces anomalies sont expliquées à la lumière d'une théorie réflexe de la cellulite proposée antérieurement.

7. Il est erroné de poser un diagnostic d'hystérie dans ces cas. Cet article se réfère aux vues de Babinski sur la paralysie réflexe et à celles de Lorente de Nó sur l'organisation sensorielle de la moëlle épinière.

THE RELATION OF THE CARDIAC LESIONS OF RHEUMATOID ARTHRITIS TO THOSE OF RHEUMATIC FEVER

BY

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The use of the term " rheumatoid " to designate one of the types of chronic arthritis reflects the persistent suspicion that this disease is somehow related to rheumatic fever. Synovitis and subcutaneous nodules occur in both rheumatoid arthritis and rheumatic fever, but we are dealing herein with the less obvious common ground of cardiac damage.

Definition for Present Discussion

For the purposes of the present discussion, the rheumatoid arthritis of childhood (Still's disease) is included, but the ankylosing spondylitis (rheumatoid spondylitis) of Marie-Strümpell is not, except when it occurs as a complication of frank rheumatoid arthritis. Also excluded are degenerative (hypertrophic or osteo-) arthritis, arthritis secondary to focal infection, and, of course, chronic specific infectious arthritis such as that due to tuberculosis. Likewise excluded for the sake of clarity are the numerous early or doubtful cases of rheumatoid arthritis, leaving only the frank, severe, late cases of this disease, whose diagnosis (based on the prominent characteristics of chronicity, tendency to symmetrical involvement, particularly of the proximal interphalangeal finger joints, and tendency to deforming contractures) is obvious and unquestionable.

Cardiac Lesions and Anaphylaxis

Baggenstoss and Rosenberg (1941) have reported from the Mayo Clinic that patients answering this description have at autopsy an abnormally high incidence of cardiac lesions which are identical with those of rheumatic heart disease. Their criteria for recognition of both rheumatoid arthritis and rheumatic heart lesions were carefully defined. This discovery has been confirmed by Bayles (1943), Fingerman and Andrus (1943), and Young and Schwedel (1944), but its interpretation has remained obscure. In discussing possible explanations, Rosenberg and others (1944) have raised the question whether rheumatoid arthritis is responsible for a form of heart disease which is indistinguishable from rheumatic heart disease, and the question whether rheumatoid arthritis and rheumatic fever are related.

A clue to this mystery may be found in the work of Rich and Gregory (1943, 1944), who were able to produce in experimental animals a carditis which closely resembled that of human rheumatic heart disease. This was accomplished simply by rendering rabbits " hypersensitive " by intravenous administration of horse serum, and the carditis was regarded as a sensitivity phenomenon analogous to anaphylaxis. Rich and Gregory (1943) inclined to the view that an anaphylactic type of mechanism is responsible for the lesions of rheumatic heart disease.

According to the generally accepted theory (cf. Boyd, 1943), the following sequence of events takes place in an anaphylactic reaction: (1) production of antibodies in response to the presence of an antigen; (2) fixation of some antibodies on or in tissue cells (sessile antibody); (3) union of sessile antibody and homologous antigen; (4) tissue response to this union, the nature of the response varying with the tissue and the animal species involved.

Antigens

While in classical rheumatic fever the antigen is probably derived from haemolytic streptococci, Rich and Gregory (1944) have suggested that *other* antigens could well give rise to lesions in man identical with those of classical rheumatic heart disease. It is the purpose of the present communication to propose that such is actually the case in rheumatoid arthritis, that is, that in rheumatoid arthritis, cardiac lesions indistinguishable from those of rheumatic fever are produced by tissue response to the union of sessile antibody and fresh antigen, the latter being necessarily homologous to the sessile antibody but presumably *different* from the

antigen in rheumatic fever. In other words, the mechanism of production of cardiac lesions is the same in the two diseases but the antigens are different. In each case, the specificity of antibody for antigen is unquestioned. Granted the entrance of fresh antigen into the circulation in suitable amounts and at appropriate intervals, the nature of the antigen is immaterial to the theory that the response of heart tissue to the union of antigen and its homologous sessile antibody represents a final common pathway of a non-specific nature.

It is obviously essential to our argument to demonstrate that the cause of rheumatoid arthritis is not the same as that of rheumatic fever. While in both diseases this awaits elucidation, enough is now known to indicate that in all probability the haemolytic streptococcus is a causative factor in rheumatic fever but not in rheumatoid arthritis. The relation of scarlet fever and haemolytic streptococcus sore throat to acute rheumatic fever and the prophylaxis of acute rheumatic fever by sulphonamides are well established. The serologic evidence has been summarized by Rantz and others (1945) with the statement that " high titres of various antistreptococcus antibodies and cutaneous hypersensitivity to products and fractions of haemolytic streptococci are usually demonstrable in persons suffering from acute rheumatic fever or from recurrences of this disease ". On the other hand, the extraordinary prolongation of the active stage of the joint lesions of rheumatoid arthritis, their tendency to symmetry, and their indifference to sulphanilamide and penicillin may be cited as evidence against a streptococcal aetiology for this kind of arthritis. The high titre of streptococcal agglutinins in rheumatoid arthritis sera has been the bulwark of the streptococcus theory of aetiology of this disease. However, the apparent strength of these agglutinins has recently been accounted for (Wallis, 1947) as being due to a non-specific enhancement of the action of normally present agglutinins. Whatever the substance eventually to be found serving as antigen in rheumatoid arthritis, the evidence at hand indicates that it is not a streptococcal derivative. It is therefore presumably different from the antigen in rheumatic fever.

In the cases reported by Baggenstoss and Rosenberg, rheumatic-type heart disease was found in 16 of 22 autopsies of frank rheumatoid arthritis, an incidence of 72 per cent., as compared with the over-all Mayo Clinic incidence of 5 per cent. In only 2 of these 16 cases had a history of rheumatic fever been obtainable. These observers noted that cardiac damage tends to be less severe (and therefore usually unrecognizable clinically) in rheumatoid arthritis than in classical rheumatic fever, and suggested that this difference might result from the fact that the onset of rheumatoid arthritis is later than the onset of rheumatic fever. They cited the general belief that the heart is more vulnerable to rheumatic infection in younger persons, and quoted evidence that in 90 per cent. of rheumatic fever cases the onset is before the age of 15, whereas in 90 per cent. of rheumatoid arthritis it is after 15. In less than half their cases had heart disease been diagnosed during life. Nevertheless, the cardiac lesions were regarded as an important contributory cause of death in 7 cases: 3 died in congestive failure, and 4 apparently died of an acute " rheumatic " inflammation. None of the latter 4 gave a history of rheumatic fever. Their ages at death and durations of arthritis were: 14 and 2 years; 24 and 2 years; 17 and 6 years; 55 and 7 years.

Young and Schwedel found an even higher incidence (33 of 38 cases, or 86 per cent.) of " rheumatic heart disease " in autopsies of frank rheumatoid arthritis. There was a history of rheumatic fever in 4 and an ante-mortem diagnosis of heart disease in 18. The cardiac lesions were regarded as an important contributory cause of death in 21. For what it is worth: in the great majority of cases in which temporal relationships could be established, the arthritis preceded the discovery of heart disease. If our interpretation is correct, the adage that " nobody dies of rheumatoid arthritis " becomes untenable.

The concept of sensitivity reactions in rheumatoid arthritis also furnishes an explanation of the presence of focal collections of round cells in the peripheral nerves and skeletal muscles in this disease. The existence of lesions of this type in the peripheral nerves was reported by Freund and others (1942). It seems likely that these cell collections have the same origin as the cardiac lesions which are under discussion, namely the result of union of fresh circulating antigen with homologous sessile antibody. This interpretation is supported by the incidence of " rheumatic " heart lesions in the same patients. Freund and his collaborators examined numerous blocks taken at autopsy from the peripheral nerves of each of 5 individuals. The largest number of cell collections in any case was 65, and this subject also had chronic rheumatic heart disease with mitral valvulitis and pericardial adhesions; the next largest number was 22, and this subject also had acute bacterial (haemolytic streptococcus) mitral and aortic valvulitis; the third largest number was 12, accompanied by a thickened mitral valve; while in the remaining 2 cases, with 5- and 2-cell collections respectively, cardiac lesions of the rheumatic type were not found. Furthermore, Freund and others quoted a report by Koeppen, who

described similar cell collections in peripheral nerves during the acute or subacute stages of rheumatic fever but not after these phases had subsided. One gets the impression that fresh antigen enters the circulation more frequently, over a longer period, and probably in smaller amounts in rheumatoid arthritis than in rheumatic fever, and also that the " sensitivity lesions " are more apt to leave permanent recognizable scars in the heart than in the peripheral nerves.

Collections of round cells have been described in the skeletal muscles of persons with rheumatoid arthritis by Steiner and others (1946). These collections were present in muscle from each of the 9 cases examined. Control specimens from 196 individuals who did not have rheumatoid arthritis failed to show these lesions, with one exception, which was from a case of subacute bacterial endocarditis superimposed on old rheumatic heart disease. Steiner and others mentioned reports by Klinge and by Graeff of the presence of cellular infiltrations in the voluntary muscles in rheumatic fever.

Designation of Heart Disease in Rheumatoid Arthritis

It is not easy to find a satisfactory designation for the heart disease which accompanies rheumatoid arthritis. " Rheumatoid arthritis heart disease " is not descriptive of the cardiac lesions. The term " rheumatoid heart disease ", used by Rosenberg and others (1944), suggests a relation to classical rheumatic carditis but fails to connote the concept of Rich and Gregory of lesions resulting from antigen-antibody union. We have avoided the word " allergy " because of its elasticity and because we do not believe that " natural hypersensitivity " (as contrasted with acquired or induced hypersensitivity) plays a part in rheumatoid arthritis. " Anaphylaxis " likewise is unsuitable because it means different things to different people, in its narrowest sense signifying a shock-like state artificially produced in some animals. The origin of the cardiac lesions under consideration is for the present probably best indicated by referring to them as the result of " hypersensitivity " or, better still, simply " sensitivity ".

Discussion of the present topic is necessarily on a speculative basis inasmuch as means have not been found for the experimental production of either rheumatoid arthritis or rheumatic fever.

Summary

It is proposed that the cardiac damage which accompanies rheumatoid (atrophic) arthritis results from the union of antigen with homologous antibody which has been previously fixed in heart tissues. As " sensitivity lesions ", these changes would be qualitatively indistinguishable from those of classical rheumatic heart disease, although the responsible antigen is apparently not the same in the two diseases. The occurrence of widespread focal microscopic lesions in other structures (peripheral nerve and voluntary muscle) in both rheumatoid arthritis and rheumatic fever is cited in support of this view.

Acceptance of this proposal would mean to the clinician that rheumatoid arthritis is a potentially fatal disease, and to the pathologist that all cardiac lesions resembling those of rheumatic fever have not necessarily the same cause.

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Rapports entre les Lésions Cardiaques de l'Arthrite Rhumatismale et celles du Rhumatisme Articulaire Aigu

Résumé

L'auteur suggère que les lésions cardiaques qui accompagnent l'arthrite rhumatismale (atrophiante) résultent de l'union d'un antigène avec l'anticorps homologue qui s'est précédemment fixé dans les tissus cardiaques. En tant que " lésions de sensibilité ", ces modifications ne se distinguent pas qualitativement de celles qui sont dues au rhumatisme cardiaque classique, bien que l'antigène responsable semble n'être pas le même dans ces deux maladies. La présence de nombreux foyers microscopiques dans d'autres tissus (nerf périphérique et muscle strié) aussi bien dans l'arthrite rhumatismale que dans le rhumatisme articulaire aigu est donnée à l'appui de cette hypothèse.

L'acceptation de cette théorie signifierait pour le clinicien que l'arthrite rhumatismale est une maladie qui peut être fatale, et pour le pathologiste que toutes les lésions cardiaques ressemblant à celles du rhumatisme articulaire aigu n'ont pas nécessairement la même cause.

A CONTROLLED SERIES OF COOKE-ARNETH POLYNUCLEAR COUNTS IN RHEUMATOID ARTHRITIS

BY

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Introduction

The Cooke-Arneth count, as a measure of the age of circulating neutrophils, is considered to be an indication of the presence or absence of active infection. For this reason, numerous studies have been made of the count in rheumatoid arthritis in order to estimate what part infection plays in this disease. Other modifications of the polynuclear count, such as the Schilling and filament-non-filament counts, which give substantially the same information, have also been employed. The results have not been entirely in agreement. Thus Hill (1931), Eaton (1932), Collins (1936), and Hartung and others (1936) have reported left shifts in a very high proportion of cases, approaching 100 per cent. Steinberg (1935) reported a left shift of the Schilling count in 78 per cent. of cases. Cecil (1933), who regarded the polynuclear count (Schilling) as " perhaps the most definite of all gauges of an infectious process ", found a left shift in 52 per cent. of cases of rheumatoid arthritis. He quoted unpublished data of Rezinoff, who found a shift to the left in 68 per cent. Kahlmeter (1938) on the other hand concluded from a study of 284 cases of rheumatoid arthritis that the infective hypothesis of its origin was unproved. This he stated as follows: " The fact that there is no increase in the total number of leucocytes nor any modification of the Arneth-Schilling blood picture is fairly strong evidence against such an (infective) hypothesis." Gray and others (1935) recorded a shift to the left in only 28 per cent. of early cases, 17 per cent. of established cases, and 15 per cent. of advanced cases.

One of the present authors (Gibson, 1938) reported the average weighted mean in rheumatoid arthritis to be significantly to the left of that of osteo-arthritis, ankylosing spondylitis, and normal persons, but in many severe and active cases normal Cooke-Arneth counts were found. The most striking finding was the wide " scatter " of the results. Cases which were clinically similar gave widely different counts. No significant correlation was seen between polynuclear count and erythrocyte sedimentation rate or haematocrit, but the unexpected result was obtained that the weighted mean was positively correlated with the neutrophil count. As the neutrophil count decreased, the Cooke-Arneth count showed an increasing left shift, and as the leucocyte count increased the shift was towards the normal. This is of interest in view of the fact that Collins (1937) reported the most marked shifts to the left to occur in cases of Felty's syndrome, in which neutropenia was a feature.

In a later study of the polynuclear count in all clinical types of rheumatism, Gibson and Kersley (1938) noted that the left shift in gout was more marked, on the average, than that in rheumatoid arthritis or in any other form of chronic rheumatism and that the difference between gout and rheumatoid arthritis was statistically significant. No one has proposed that gout is an infective disease, but these results suggested that a metabolic toxaemia, or tissue reaction to toxic trauma, as found in gout, can produce a left shift of the polynuclear count.

In view of these discrepancies and apparent anomalies it was thought that further information of value might be derived from series of counts made in cases of rheumatoid arthritis which were (a) clinically typical (b) of duration under five years, the series being controlled by counts made in the same town on non-rheumatic persons of the same age, sex, and social status suffering from non-infective lesions of the locomotor system. These were for the most part convalescent orthopaedic cases in a general hospital. The aim was to assess whether a left shift of the Arneth count occurred in cases of rheumatoid arthritis, and, if so, whether it could be taken as evidence that this disease was the result of an infective process.

Methods

Films were made from venous blood and slides were stained by Leishman's method. All counts were made by the same person (H. J. G.) and the criteria for classification proposed by Cooke and Ponder (1927) were rigidly followed. The " weighted mean " which expresses the result of each count is the mean number of lobes per nucleus in the neutrophil polymorphonuclear leucocytes. The question of what constitutes a normal polynuclear count is a complex one. Evidence has been quoted previously (Gibson, 1938) which indicates that the normal varies considerably in different parts of the world, possibly as a result of climatic conditions. In Bath the average weighted mean in fifty-five healthy persons was 2·43. Subsequent experience over nine years has shown that this is a serviceable standard for routine use in general work. It must be emphasized that the controls in this study were not normal healthy persons at work, but that they were, as far as clinical examination showed, free from any infective disease.

The blood sedimentation rate in both series was estimated by the Westergren method, the figure quoted being the millimetres fall in one hour.

Results

General Comparison of Case and Control Series.—In Table 1 the results are classified in five groups. Five rheumatoid cases showed very marked shifts to the left with weighted mean under 1·60. No controls were found in this group. At the other end of the scale cases were more numerous than controls in the strictly normal group with weighted means of 2·50 to 2·79 and in the intermediate group 2·20 to 2·49 which may be regarded as a mild left shift merging into the normal. Finally in the group of weighted mean 1·60 to 2·19, showing a definite left shift, controls were much more numerous than cases, the figures being 28 and 18 respectively. The averages of the weighted means was 2·14 for cases and 2·16 for controls, a negligible discrepancy. Thus, the only difference between the groups was one of distribution, the rheumatoid series showing a wider scatter than the controls, which were more closely grouped about the mean (see Figure).

TABLE 1

FREQUENCY DISTRIBUTION OF WEIGHTED MEANS IN RHEUMATOID ARTHRITIS CASES AND IN CONTROLS

Weighted mean range	Number of cases	
	Rheumatoid arthritis	Controls
1·30–1·59	5	0
1·60–1·89	8	10
1·90–2·19	10	18
2·20–2·49	18	16
2·50–2·79	9	6

It may be noted that the previous series reported by Gibson (1938) gave the average number of lobes per neutropnil in 345 cases of rheumatoid arthritis as 2·245. In that series there was a predominance of very old-standing cases, the normal population of a rheumatic diseases hospital. The present series included only relatively early cases.

Further Analysis of Rheumatoid Arthritis Group.—It was desired to find whether the widely varying counts in the rheumatoid group could be correlated with any other feature of the case. Thus, if a left shift were directly related to aetiology it might be expected to vary with activity as shown by the erythrocyte sedimentation rate.

The relevant figures are given in Table 2. It will be seen that in each blood sedimentation rate group a wide range of weighted means is represented and, in view of the small numbers in some of the groups and the wide scatter of the figures, the average weighted mean is relatively constant. It shows no tendency to rise or fall in a regular way with increasing sedimentation rate. The results confirm the absence of correlation in the large series reported by Gibson (1938).

Duration of the Disease.—The duration of the disease and its

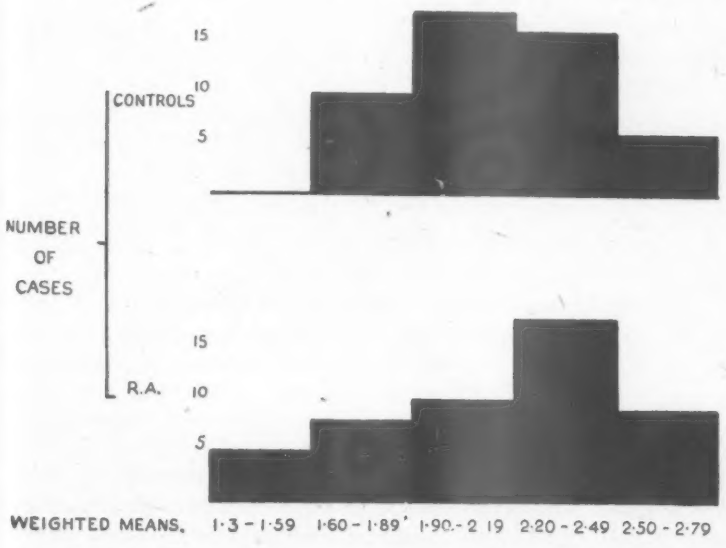

FIGURE.—Frequency distribution of weighted means of Cooke-Arneth counts in cases of rheumatoid arthritis and in controls.

TABLE 2

ARNETH COUNT AND ERYTHROCYTE SEDIMENTATION RATE (WESTERGREN METHOD) IN RHEUMATOID ARTHRITIS CASES

E.S.R. mm. fall in 1 hr.	No. of cases	Range of weighted mean	Average weighted mean
9	4	1·52–2·41	2·178
10–19	15	1·82–2·64	2·216
20–29	9	1·59–2·55	2·316
30–39	8	1·36–2·62	1·940
40–49	6	1·61–2·54	2·240
50–59	1	—	1·910
60–69	4	1·41–2·15	1·745
70–79	1	—	2·170
80–89	2	1·81–2·32	2·065
—	50	1·36–2·64	2·140

TABLE 3

ARNETH COUNT AND DURATION OF RHEUMATOID ARTHRITIS

Duration of disease (years)	No. of cases	Range of weighted means	Mean weighted means
Under 1	12	1·55–2·55	2·16
1–2	15	1·36–2·64	2·07
2–3	13	1·41–2·54	2·17
3–4	3	1·83–2·41	2·13
4–5	7	1·66–2·62	2·18
Up to 5	50	1·36–2·64	2·14

relation to polynuclear count is shown in Table 3. The average weighted mean remains practically constant, with no tendency to increase or diminish within the five-year period. In each group high and low weighted means are represented.

Age of Patient.—Table 4 shows that a similar wide range of values is included under each age period and that the average weighted mean is remarkably constant except when the number of cases is very low, as in the 60 to 69 age group.

Sex of Patient.—This is shown in Table 5. Although females show a more marked shift on the average than males, the range in each group is very wide and chance would account for the observed differences.

Results Expressed in Terms of the Non-filament Count.—In view of the fact that the non-filament–filament count of Farley and others (1930) has been used by a number of workers in the United States, our figures have been calculated to express the results in that form, class one of the Cooke-Arneth count being the non-filament percentage. The average non-filament count was 26·5 per cent. in the rheumatoid group and 24·2 per cent. in controls. The normal non-filament percentage is 16 or less. Applying this standard we find that 32 of the case series had a left shift as compared with 33 controls. The difference is insignificant. This form of the polynuclear count did not, therefore, give a result materially different from the more inclusive Cooke-Arneth count. Haden (1935) has pointed out that the Schilling and non-filament counts emphasize the immature forms while the Cooke-Arneth, which takes into account neutrophils of all ages, places emphasis on the more mature cells. In the present series the results are the same by both methods.

TABLE 4

AGE OF PATIENT AND ARNETH COUNT IN RHEUMATOID ARTHRITIS

Age	No. of cases	Range of weighted mean	Average weighted mean
<19	5	1·55–2·55	2·060
20–29	7	1·41–2·62	2·160
30–39	8	1·36–2·55	2·083
40–49	16	1·52–2·64	2·210
50–59	12	1·59–2·55	2·063
60–69	2	2·17–2·54	2·355
—	50	1·36–2·64	2·149

TABLE 5

SEX OF PATIENTS AND ARNETH COUNT IN RHEUMATOID ARTHRITIS

Sex	No. of cases	Range of weighted mean	Average weighted mean
Male ..	20	1·36–2·62	2·223
Female ..	30	1·41–2·64	2·093

Summary of Results

Arneth Count.—Adopting the standard used by Collins (1936), if all counts with weighted mean of less than 2·40 are regarded as showing a left shift our results show such a shift in 72 per cent. of rheumatoid cases and 76 per cent. of controls. Our own standard in routine blood counting is less stringent. From an experience of many thousands of counts made in general medical and surgical cases at Bath, we are inclined to regard any weighted mean of 2·30 or more as normal. On this standard

58 per cent. of rheumatoid cases and 64 per cent. of controls show a left shift.

Non-filament Count.—This method indicated that 64 per cent. of rheumatoid cases and 66 per cent. of controls showed a left shift.

By all methods the proportion of left shifts is greater in controls but the difference is not significant. The proportion of abnormal counts in rheumatoid cases is in general agreement with that found by a number of previous workers, but its significance is completely modified by the finding of an equal number of abnormal counts in controls.

Discussion

The most striking feature of the results is the high incidence of left shift in the control series and the close agreement between the results in cases and controls. All counts were made by one of us (H. J. G.), and so no error due to change of standards is involved. Throughout the whole duration of this study polynuclear counts have been made as a routine on general and rheumatic cases and the general run of results of these counts has been the same as during the past twelve years. The seasons involved were from November, 1946, till September, 1947, and included the severe weather early in 1947. The only notable epidemic was that of poliomyelitis, but no cases of this were found in the rheumatic hospital nor were any encountered in the general hospital where the controls were situated. The incidence of subclinical infection is an unknown factor. It may have influenced the figures in both groups.

In comparison with previous work the incidence of left shifts in our series occupies an intermediate position. It is higher than that reported by Gray and others (1935) and Kahlmeter (1938), and is of a similar order to the findings of Steinberg (1935), Cecil (1933), Rezinoff (1933) and of Short and others (1937) for cases of under one year's duration, but lower than the 93 per cent. noted by these workers for cases of more than one year's duration. The standard used by the last-named was very rigid. Combining myelocytes, juveniles, and band forms, they calculated these young cells as a percentage of total polymorphs and regarded more than 8 per cent. as indicative of a left shift. If we apply this standard to the present series all the rheumatoid cases would show a left shift as compared with 92 per cent. of controls.

Our case incidence of left shifts is very much below those reported by Hill (1931), Collins (1936), Steinbrocker and Hartung (1933), and Hartung and others (1936). When these discrepancies are scrutinized it is seen that the apparently great difference may be due partly to differences in interpretation and partly to sampling errors where results show such marked variation as they do in rheumatoid arthritis. Thus Collins found the average weighted mean in 39 female patients to be 2·14 and in 10 males to be 2·11, or 2·13 overall. This is practically the same as our average for the case series of 2·14. He regarded a weighted mean of 1·95 to 2·09 as a " marked left shift " and less than 1·95 as a " severe left shift ". It may be noted that in enteric and abortus fevers, acute virus infections, and active tuberculosis, figures of the order of 1·05 to 1·4 are not uncommon. Thus our impression of a severe shift to left is a much more marked deviation than Collins describes.

Left shift of the polynuclear count is not necessarily indicative of infection. It is physiological in pregnancy and may be found following surgical operations and fractures where infection may be excluded. Tissue reaction of this kind may well account for the left shift in our control series. It is also the rule in many blood diseases and a familial form has been described by Peterson (1935). Again chemical toxaemia may also give rise to a left shift, either by destruction of more mature cells or by inhibition of maturation. Gout has already been mentioned. A recent case of sulphonamide intolerance with fever and skin rash yielded an Arneth count of 1·16. Three cases of thiouracil intolerance seen by one of us (H. J. G.) showed weighted means of 1·73, 1·12, and 1·09 when the neutrophil counts were 1420, 396, 22 per c.mm. respectively. The similarity between these cases and the Felty group of rheumatoid arthritis in which Arneth left shift accompanies neutropenia is interesting.

The results of the present series show that there is no significant difference between the results of polynuclear counts in cases of rheumatoid arthritis and in controls in whom non-infective lesions of the locomotor system (old fractures) were present. Whether shifts are due to unrecognized septic foci, intercurrent infections, tissue reaction to aseptic inflammation, trauma, or chemical toxaemia, the rheumatoid arthritic cases showed no greater evidence of neutrophil reaction than did the non-rheumatic controls. The results argue against a direct infective aetiology of rheumatoid arthritis. The fact that the counts in this series showed no constant relation to activity or to duration is further evidence in the same direction. From the clinical point of view scrutiny of the case records repeatedly showed that an active case with widespread and severe rheumatoid involvement presented a normal count. This finding is quite unlike the results of similar counts in tuberculosis, syphilis, endocarditis lenta, or other true infections.

Summary and Conclusions

Cooke-Arneth polynuclear counts have been made on fifty cases of rheumatoid arthritis, all typical in their clinical manifestations and of under five years' duration. They are compared with counts made by the same person on fifty controls of the same age and sex who were for the most part convalescent orthopaedic (fracture) cases.

No significant difference was noted between the results in cases and controls.

In the rheumatoid arthritis group no correlation was present between the polynuclear count and age, sex, erythrocyte sedimentation rate, clinical severity, or duration of the disease.

The results afford no support to the view that rheumatoid arthritis is the direct result of micro-organismal infection.

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Série Comparée de Numérations de Polynucléaires de Cooke-Arneth dans l'Arthrite Rhumatismale

RÉSUMÉ

On a fait des numérations de polynucléaires de Cooke-Arneth dans cinquante cas d'arthrite rhumatismale présentants tous des manifestations cliniques typiques et présentes depuis moins de cinq ans. Elles sont comparées avec des numérations faites pat la même personne sur cinquante témoins du même âge et du même sexe qui sont pour la plupart des convalescents de fractures.

On n'a constaté aucune différence significative entre les résultats obtenus pour les malades et pour les témoins.

Dans le groupe d'arthrite rhumatismale il n'existait aucune corrélation entre la numération des polynucléaires et l'âge, le sexe, le taux de sédimentation érythrocytaire, la gravité clinique ou la durée de la maladie.

Ces résultats n'apportent aucune confirmation à la théorie selon laquelle l'arthrite rhumatismale est le résultat direct d'une infection microbienne.

THE PHOSPHATASE ACTIVITY IN SPONDYLITIS ANKYLOPOIETICA

BY

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Introduction

Ankylosing spondylitis is at present a disease of unknown aetiology and many theories have been put forward as to its origin. Buckley (1945) reviewed a mass of evidence bearing on a possible biochemical mechanism which involves serum phosphatase as a cardinal factor in producing the abnormal ligamentous calcification and the bony changes which constitute the main pathological features of the disease. Batson (1940), investigating the spread of carcinoma of the prostate to the sacro-iliac regions and spine, suggested that the venous plexus connecting the prostatic veins with the prevertebral veins might well be the route of spread of metastases. Cunningham (1937) described a venous plexus between the periosteum and spinal canal. These veins, being without valves, may produce stagnation of blood in these regions and cause meningeal irritation. Ludwig and others (1943) reported an increase of protein and abnormal Lange curves in forty-two cases based on a study of 101 cases of spondylitis ankylopoietica.

The prostate contains a very active phosphatase. This phosphatase can be estimated in the blood as it has its optimum activity at a *p*H of 4·9. Normal amounts lie between 1 and 3 units. Gutman and Gutman (1938) found that very large amounts of acid phosphatase may appear in the blood in carcinoma of the prostate with secondaries in the bones. McWhirter (1945), considering that a leakage of prostatic acid phosphatase into the prevertebral veins may be an aetiological factor in the production of spondylitis, investigated the acid serum phosphatase in seven patients and found a raised level in cases in which the disease was at an early stage. Shorvon and Pearson (1937) reported a raised acid phosphatase in one early case of several cases investigated, but did not give the total number of cases under review. Race, quoted by Buckley (1945), estimated the acid phosphatase in thirteen cases and found that the average level was 2·2 units (normal 4 units). The highest figure was 3·8 and the lowest 0·9 units, and Race concluded that acid phosphatase probably had no bearings on ankylosing spondylitis. In a series of cases reported by him in 1945 Buckley found a slight increase in the alkaline phosphatase, the average being 0·35 (Kay units) compared with the normal maximum of 0·2 units. Race, in 1932, estimated the alkaline phosphatase in sixteen cases and reported a slight rise, between 0·21 and 3·6 units in seven cases (43·7 per cent). Normal 0·11 to 0·19 (Kay units).

In view of the conflicting reports as to the value of estimating the alkaline and acid phosphatase in

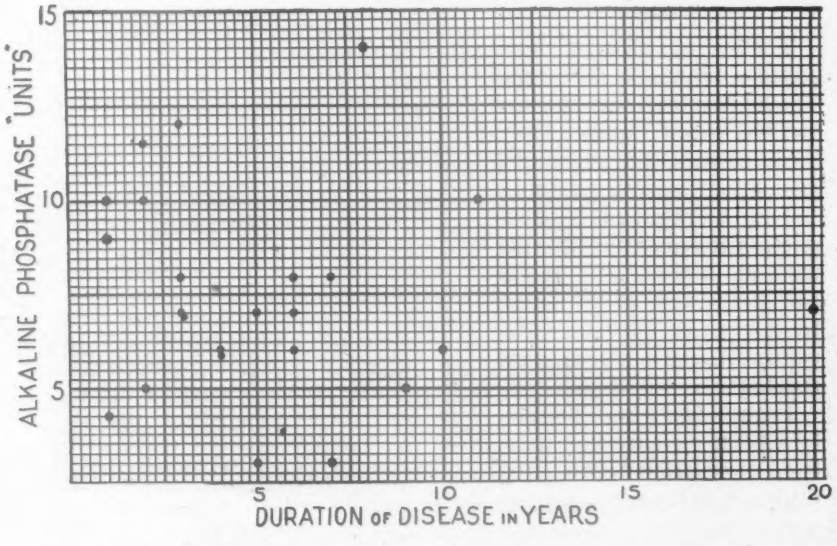

FIG. 1.—Scatter diagram showing lack of correlation between duration and alkaline phosphatase.

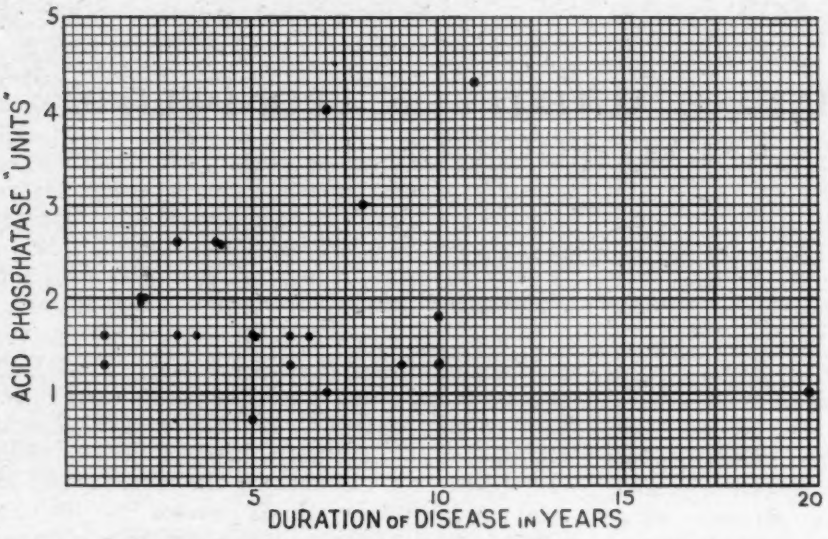

FIG. 2.—Scatter diagram showing lack of correlation between duration and acid phosphatase.

cases of spondylitis ankylopoietica and the different methods used, a series of twenty-four cases was investigated.

Method

The method used was King's (1946) modification of King and Armstrong. It depends on the amount of phenol set free when the enzymes are allowed to act on an ester of phosphoric acid such as phenyl phosphate at an optimum *p*H. The normal levels by this method are 5 to 10 units and 1 to 3 units for the alkaline and acid phosphatases respectively.

Results

The average alkaline phosphatase level was 6·2 units. The highest level was 14 units and the lowest 3 units. Only three cases (12·5 per cent.) gave a high normal reading.

The average acid phosphatase activity was 1·75 units with the highest level at 4·3 and the lowest at 0·7 units. In this series two cases (8·5 per cent.) gave a high normal reading.

From Figs. 1 and 2 it can be seen at a glance that there is no correlation between the duration of disease in years and the alkaline and acid phosphatase activity.

Figs. 3 and 4 are scatter diagrams showing the lack of correlation between the alkaline and the acid phosphatase and the activity of the disease. The sedimentation rate is a good index of activity, being raised in the active stage and tending to reach normal as the condition becomes arrested.

Discussion

Osteoporosis is an early recognizable change in spondylitis. This may be associated either with an increase osteoclastic activity or a reduced osteoblastic action in the bone. As a result of the bone-softening it is possible that the calcification which takes place in the fibrous and fibro-cartilaginous structures round the affected joints may be an attempt at splinting the softened bones to prevent deformity.

Sclerosis, an early radiological change in the sacro-iliac and intervertebral joints is usually associated with relatively low values of serum phosphatase activity, whereas in osteoporosis of rickets the phosphatase is consistently raised and tends to return to normal during antirachitic therapy (Bodansky and Jaffe, 1934). These three antagonistic processes of osteoporosis, osteosclerosis,

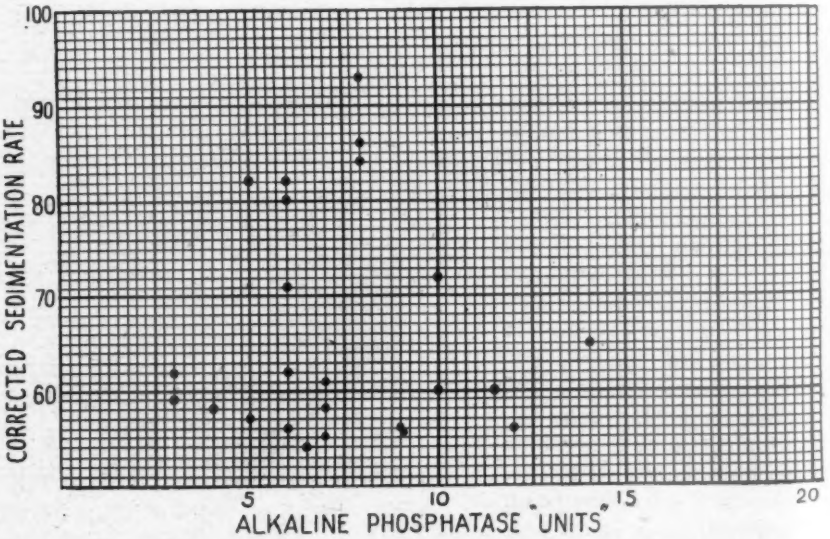

FIG. 3.—Scatter diagram showing lack of correlation between corrected sedimentation rate and alkaline phosphatase.

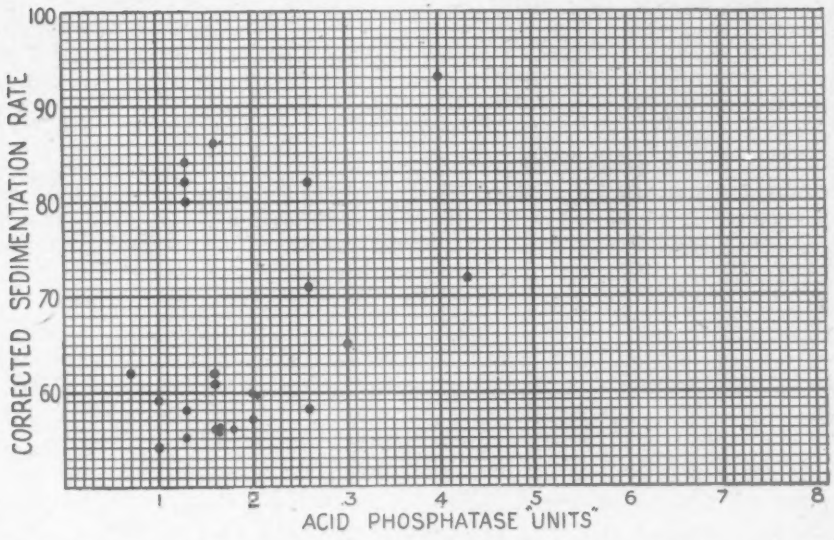

FIG. 4.—Scatter diagram showing lack of correlation between C.S.R. and acid phosphatase.

and calcification of ligaments taking place simultaneously may be the cause of frequent normal values for the serum phosphatase, and the occasional high values reported may be due to the predominence of osteoblastic activity at the time of estimation. There is also some evidence that senility, malnutrition, and anaemia tend to lower the serum phosphatase activity (Cantarow and Trumper, 1945); and the influence of the parathyroid hormone, thyroxin, vitamin D, and absorption of calcium from the bowels should be borne in mind in interpreting the complicated processes of calcium metabolism.

Summary

1. The literature on the estimation of serum phosphatase in spondylitis ankylopoietica is reviewed.

2. The relation between alkaline and acid phosphatase and the duration and activity of the disease is discussed.

3. It is suggested that the simultaneous and directly opposite processes of osteoporosis on the one hand, and sclerosis with abnormal calcification of ligaments on the other, are a cause of the frequent normal values for the serum phosphatase activity.

I wish to express my indebtedness to E. W. Richardson, Laboratory Technician at the Royal National Hospital for Rheumatic Diseases, Bath, for his help in carrying out the estimations.

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Activité des Phosphatases dans la Spondylite Ankylosante

RÉSUMÉ

1. Revue bibliographique sur le dosage de la phosphatase dans la spondylite ankylosante.

2. Discussion sur le rapport entre la teneur en phosphatase alcaline et en phosphatase acide et la durée et la gravité de la maladie.

3. L'auteur suggère que les processus simultanés et directement opposés d'ostéoporose d'une part, et de sclérose avec calcification anormale des ligaments de l'autre, sont responsables des valeurs fréquemment normales de l'activité phosphatasique du sérum.

THE CAMPAIGN AGAINST RHEUMATISM

In a most stimulating article in the *Annals of Internal Medicine* (February, 1948, p. 368) Dr. P. S. Hench calls attention to the vastness of the problem in America and this country and the necessity for more support, both from the Governments and from the public if this scourge is to be tackled adequately.

" In every country the same findings have been made: (1) rheumatic diseases outrank all others as a cause of chronic morbidity; (2) rheumatic disease annually involves each country in great expense; (3) adequate facilities for the care of most rheumatic patients are non-existent."

Hench quotes staggering figures for the United States and compares their prospects with those of others, " for example for 680,000 tuberculous patients there are available about 100,000 free beds and 100,000,000 dollars annually for care and research but for 6,850,000 rheumatic patients there are available only about 200 free beds and 200,000 dollars annually for care and research. In other words, although there are ten times as many rheumatic as tuberculous patients, the latter have available 500 times more beds and money. Thus the tuberculous patient, happily thereby a vanishing race, receives 5,000 times as much attention as the non-vanishing rheumatic."

He points out that a survey of voluntary health agencies in America discloses the astonishing paradox that " the greater the need the less the public support " but considers that this is due simply to the fact that the public has not been sufficiently informed or aroused (see Table).

Turning to this country the writer comes to the same conclusions. " In England and Wales before the war there were 30,000 beds for tuberculous patients and only 1,000 for the rheumatic "; and he quotes the well-known fact that rheumatism costs the people of England and Wales 25 million pounds annually and constitutes " the greatest single enemy of social well-being and economic efficiency in Great Britain ". It is " a major health problem in Scottish industrial life ".

" In Sweden where most workers are insured, rheumatic cripples become pensionable and were doing so at the rate of 5,000 each year."

Dr. Hench reviews the progress made and the setback caused by the war to the campaign against rheumatism. Many rheumatism societies have been formed in America and there are " scores " of rheumatism clinics, whereas before 1910 there were none. The membership of the American Rheumatism Association is now more than 400. Whereas in this country physicians with a special knowledge of the rheumatic diseases were employed during the war in general medical duties, those in the American Services were wisely used on more specialized duties so that certain clinical studies were continued.

In 1936 the Canadian Rheumatism Association was formed and has a close liaison with the American Association as well as being part of the Pan-American League Against Rheumatism.

Dr. Hench has many kind words to say about the Empire Rheumatism Council; for its plans, for its achievement in obtaining an assurance from the Government that rheumatic patients will be fully

TABLE

DISEASE PREVALENCE VERSUS VOLUNTARY PUBLIC SUPPORT

Disease	Support	Amount collected " annually "	Patients	Dollars available per patient
Infantile paralysis ..	Sold to public	$16,600,000	175,000 crippled	94·00
Tuberculosis ..	Sold to public	$15,000,000	680,000	22·00
Cancer	Partly sold to public	$4,000,000	500,000 under treatment	8·00
Diabetes	Not sold to public	$30,000	660,000	·05
Heart disease ..	Not sold to public	$100,000	3,700,000	·03
Rheumatism and arthritis ..	Not sold to public	?	6,850,000	?

provided for under the National Health Act, and for its efforts in the fields of education and research. He points out that the *Annals of Rheumatic Diseases* is the only European journal dealing specifically with the problem of rheumatism. "Above all the Council has effectively aroused British public opinion, the controlling force of official action."

The article will be a source of stimulus and encouragement to workers in this difficult field throughout the world. One cannot do better than quote the final paragraph in its characteristic vein. "Regardless of details the international campaign is proceeding and is succeeding modestly. To 'rheumatology' more and more physicians are devoting much or all of their time. But for full success the public must support these physicians. It is not correct to say that the public gets only what it wants or deserves and that if the public really wanted a cure for rheumatism or cancer it could obtain it by adequate support. Even with the latter the public could hardly 'buy' the remedy in a year or a decade. But unfortunately much of the rheumatic public ignores the useful remedies now available. Individual initiative being what it is, the public has largely received benefits it did not request. It did not ask for the telephone, automobile, or radio. But for good or ill it got them. Thus national action is largely of value as it enhances the opportunities of the individual worker and utilizes his contributions. To that all-important end united effort must be obtained."

OSWALD SAVAGE.

ABSTRACTS

[This section of the JOURNAL *is published in collaboration with the two abstracting Journals,* Abstracts of World Medicine, *and* Abstracts of World Surgery, Obstetrics and Gynaecology, *published by the British Medical Association. The abstracts are divided into the following sections: acute rheumatism; articular rheumatism (rheumatoid arthritis, osteo-arthritis, spondylitis, miscellaneous); gout; non-articular rheumatism; general articles. After each subsection of abstracts follows a list of articles that have been noted but not abstracted. Not al sections may be represented in any one issue.*]

Acute Rheumatism

Studies on the Pathogenesis of Rheumatic Fever. I. Experimental Production of Autoantibodies to Heart, Skeletal Muscle and Connective Tissue. II. Cardiac Lesions Produced in Rats by Means of Autoantibodies to Heart and Connective Tissue. CAVELTI, P. A. (1947). *Arch. Path.*, **44**, 1.

Streptococci and staphylococci alter extracts of certain tissues so that they become antigenic to animals of the same species—that is, become auto- or iso-antigens according as they act in the same individual or in another animal of the same species. The antibodies produced by injecting simple mixtures of *killed* organisms and tissue extracts into animals of the same species react with the microbe and also separately and specifically with the tissue extract. The author demonstrates the development of antibodies against iso-antigens obtained from rat muscle and connective tissue (he used the celloidin particle agglutination technique). He describes lesions in the heart valves of the injected rats which he regards as due to damage by the anti-connective-tissue antibodies. They have some resemblance to rheumatic lesions, and the author considers that damage by antibodies to connective-tissue auto-antigens plays a part in the pathogenesis of rheumatic carditis in man. He also claims that glomerular nephritis produced in earlier experiments by the simultaneous injection of killed streptococci and kidney extract was due to the development of antibodies against kidney autoantigens. *D. M. Pryce.*

Studies in the Pathogenesis of Rheumatic Fever. The Antistreptolysin Titre in Acute Tonsillitis and Rheumatic Fever. [In English.] WINBLAD, S., MALMROS, H., and WILANDER, O. (1947). *Acta med. scand.*, Suppl. 196, 533.

The antistreptolysin titre was investigated in 71 cases of acute sore throat, estimations being made in the acute stage and also serially during convalescence. The subjects were 67 student nurses or female hospital employees between the ages of 15 and 35, and 4 males. The antistreptolysin titres were estimated by Ipsen's (*Acta path. microbiol. scand.*, 1944, **21**, 203) modification of Kalbak's method, readings being made during the acute stage and once a week in convalescence. Cultures were also made from the throat during the acute stage. A reading of 200 units or higher was considered to indicate an elevated antistreptolysin titre, and 52 cases showed such elevation at some time during the period of observation. The titre in 15 of the remaining 19 cases showed slight depression, or no alteration at all, during serial observations. In the remaining 4 cases there was a low initial titre—under 50 units—but this rose to 170 to 180 units during the course of observation. Cases with high initial titres tended to develop the highest maximum titres.

Rheumatic complications were observed in 14 cases, in 7 of which the diagnosis was based on the occurrence of transitory pains in one or more joints, while in the other 7 there were " more pronounced joint pains and rheumatic changes in the joints, as well as other symptoms which justify the diagnosis of rheumatic fever ". In 12 cases there was an initial antistreptolysin titre of 140 units, and in 9 a titre of 200 units or more. This was considered probably to be due to previous infections with haemolytic streptococci, and it is suggested that such patients are particularly liable to develop rheumatic complications. There was an initial titre of 140 units or higher in 35 cases. Septic complications, such as tonsillar abscess, otitis, sinusitis, or lymphadenitis, occurred in 3 of the 15 cases which showed no elevation of the antistreptolysin titre, and in 20 of the cases in which the titre did rise. When the complications occurred there was often, but not always, an increase in the titre. Estimations of the erythrocyte sedimentation rate were carried out; nothing of unusual interest emerged from the results. *R. B. Lucas.*

" Albumin-Bacterioplasma Conjugates " with Special Reference to the Etiology of Rheumatic Fever. A Preliminary Report. SCHULTZ, M. P., and ROSE, E. J. (1947). *Publ. Hlth. Rep., Wash.*, **62**, 1009.

Observations are recorded on the properties of toxic combinations between tissue fluids or blood serum and components of living haemolytic streptococci—called albumin-bacterioplasma conjugates, which suggest that such substances may be concerned in the pathogenesis of rheumatic fever. By a series of tests of the several serum components it is shown that the albumin of human serum is chiefly responsible for the formation of toxic conjugates. Human plasma fractions prepared by precipitation with alcohol in the cold were dissolved in normal saline.

Several observations suggest that these conjugates may be concerned in the aetiology of rheumatic fever. Thus, 47 strains of Group A *Streptococcus pyogenes* from various sources were used to prepare conjugates: 23 yielded lethal extracts, and of these 15 were from rheumatic fever patients; of the other 24, only 5 were of this origin. Again, a degree of protection against the lethal action of the conjugates in mice was obtained when the

conjugate was previously treated with serum from rheumatic fever convalescents; this property was found in 9 of 16 such sera. In several species of laboratory animals parenteral administration of conjugates prepared by using homologous serum or albumin fractions resulted in the development of cardiac lesions closely resembling those of rheumatic fever. Further, rheumatic fever patients and convalescents are hypersensitive to exceedingly small doses of these conjugates, reacting by slight fever, leucocytosis, and increased erythrocyte sedimentation rate, and, in 1 case, by the apparent activation of the arthritic and carditic rheumatic process.

Kenneth Stone.

Effect of Para-Aminobenzoic Acid on Fever and Joint Pains of Acute Rheumatic Fever. ROSENBLUM, H., and FRASER, L. E. (1947). *Proc. Soc. exp. Biol., N.Y.*, **65**, 178.

Because of its effect in rickettsial diseases, *p*-aminobenzoic acid was tried in acute rheumatic fever. The substance appeared to have an effect on the fever and joint pains in 9 patients (ranging in age from 6 to 12 years) who were given an initial dose of 3 to 4 g. at 2- to 3-hourly intervals. *R. Wien.*

Cerebral Manifestations of Acute Rheumatic Fever. WARREN, H. A., and CHORNYAK, J. (1947). *Arch int. Med.*, **79**, 589.

The author's conclusions from a study of the literature and of 207 patients with rheumatic fever, of whom 5 exhibited cerebral disturbance, are as follows. Apart from and distinct from chorea, there may occur in the course of rheumatic fever a series of manifestations of higher cerebral disturbance, including hallucinations, phobias, and sharp and intense panic; also cerebral manifestations of the peripheral embolic phenomena of bacterial endocarditis; and a group comprising delirium, restlessness, and convulsions. There is a syndrome in rheumatic fever consisting of mask-like facies, mental retardation, and sleeplessness. Lastly, the possibility of salicylate intoxication must be kept in mind.

G. F. Walker.

Rheumatic Fever Recurrences in Children without Sulfonamide Prophylaxis: An Evaluation of Environmental Factors. JACKSON, R. L., KELLY, H. G., ROHRET, C. H., and DUANE, J. M. (1947). *J. Pediat.*, **31**, 390.

This study from the State University of Iowa was undertaken in order to determine whether recurrence of rheumatic fever could be prevented by maintaining an optimal environment for the patient, or whether sulphonamide prophylaxis was always indicated.

A total of 266 children whose rheumatism began between 1930 and 1946 were given instructions about diet, clothing, avoidance of infections, rest, and sleep. They were studied for an average period of 3½ years, during which 51 children had 71 rheumatic relapses. Recurrence rates at different ages were compared with those in a control series of 134 rheumatic children to whom no such instruction were given. A further comparison was made with the figures given by Wilson (*J. Amer. med. Ass.*, 1944, **126**, 477) for the expected rate of recurrences in a random sample of rheumatic children. It was found that the children of 4 to 14 years who were given this special instruction suffered significantly fewer relapses than either control series. Aboye the age of 14 the " treated " cases fared no better than the controls. The various environmental factors were then evaluated separately by means of a chi-square test, the economic status, social status—that is, degree of parental co-operation—and diet of each patient being assessed by a social worker. The recurrence rate was found to be significantly dependent on the patient's diet but not upon his economic or social status (many of the poorer children received an improved diet through outside aid). From the low rate of recurrences when a rheumatic child received a good diet it is concluded that sulphonamide prophylaxis is indicated particularly where a good diet cannot be procured. *D. Gairdner.*

The Prevention of Rheumatic Fever in Children by the Use of Sulfonamides. LYON, R. A., RAUH, L. W., and WOLF, R. E. (1947). *Ohio St. med. J.*, **43**, 394.

In a previous paper (*J. Pediat.*, 1945, **27**, 516) the authors reported their experience of the use of sulphonamides in the prevention of recurrences of rheumatic fever. None of the original group of 70 children observed for 81 patient-seasons had a recurrence. In the present paper they report the results of the continued treatment of the same 70 children together with 50 new patients. In all, 120 children were treated for a total of 177 patient-seasons. There was no control series. Patients were treated either at a convalescent home, at a school for crippled children, or at special out-patient clinics. In the last group treatment was sometimes irregular. The daily dose was 0·5 g. of sulphathiazole (101 cases) or sulphadiazine (92 cases). Treatment was stopped when toxic reactions developed; this occurred in 37 out of 193 patient-seasons. Albuminuria was the most common complication and occurred in 23 instances. In a certain proportion of the cases during the 4 summer months treatment was withheld. There were 12 recurrences, 8 after therapy had ended (after an average time of 4½ months since treatment was stopped). Two patients had not been receiving treatment regularly; 2 had had regular treatment for 3 weeks and 1 month respectively.

The authors do not doubt the efficacy of the sulphonamides as prophylactic agents. They make a suggestion that children with permanent valvular damage should be maintained on prophylactic doses for 3 to 4 years, and that children over 15 with little or no cardiac damage should have this treatment for 2 years. *H. A. Burt.*

Periarteritis Nodosa with Enterococci on Blood Culture, associated with Acute Rheumatism. (Périartérite noneuse avec hémocultures positives à l'entérocoque associée au rhumatisme articulaire aigu.) KAUFMANN, H., and DELAUNAY, A. (1947). *Bull. Soc. méd. Hôp. Paris*, **63**, 1075.

Acute Rheumatic Infection without Articular Localization and with the Early Syndrome of Partial A-V Block. (Infezione reumatica acuta senza localizzazioni articolair con sindrome precoce di blocco parziale atrio-ventricolare). DI MARIA, G. (1948). *Rif. med.*, **62**, 4.

Fever Therapy of Chorea. BENITEZ, A. I., and DE LA CERDA, R. A. (1947). *Rev. chile. Pediat.*, **18**, 661.

Rheumatic Fever. AKENHEAD, W. R. (1948). *Amer. Practit. Phila.*, **2**, 405.

Articular Rheumatism
(Rheumatoid Arthritis)

A New Treatment of Rheumatoid Arthritis. BARSI, I. (1947). *Brit. med. J.*, **2**, 252.

The author observed that 3 cases of severe arthritis of the rheumatoid type were much benefited by intercurrent pregnancy, although the improvement ceased after parturition. He mentions that similar cases have been observed by others, and that Hench collected the records of 37 pregnancies in 20 women, in all of whom such improvement was seen temporarily. This suggested to him that there was some specific substance circulating in the blood during pregnancy which could be utilized for the treatment of cases of rheumatoid arthritis. He reports the results of transfusion of the blood of pregnant women into patients with severe rheumatoid arthritis, both male and female; 300 ml. of citrated blood was given on several occasions. There was great improvement in 64% of 28 cases subjected to this treatment. The author describes 6 cases. The major improvement occurred on the day after the first transfusion, and in several instances was preceded by a considerable rise in temperature which followed the transfusion.

[The method would seem to be a difficult one to apply on a large scale, and there would appear to be no reason why its effect should be lasting. According to the author, however, there are some cases " which can be promptly and permanently cured " in this way. He does not deal with the possibility that mild protein shock may explain the beneficial effect in view of the reported pyrexia after transfusion in some of the cases. There were no control cases.] *W. S. C. Copeman.*

The Treatment of Rheumatoid and Infective Arthritis by the Sulphonamides, with Special Reference to " Proseptasine ", Sulphadiazine and Sulphaguanidine. PARR, L. J. A., and SHIPTON, E. A. (1947). *Med. J. Aust.*, **1**, 323.

Small doses of sulphonamide drugs were given over a long period of time to patients with rheumatoid arthritis. Seventy cases are discussed. Of the 51 treated with sulphonamides alone, 21 were considered cured and 17 improved. In 19 cases in which both gold and sulphonamides were given, 5 were reported cured and 10 improved. There was 1 death from panmyelophthisis in a patient who received gold and sulphonamides. Twelve patients developed a rash, those with small or moderate increase in the erythrocyte sedimentation rate (E.S.R.) being more likely to develop a rash than those whose E.S.R. was high. The criteria of cure appear to have been strict—namely, loss of symptoms, gain in weight, and return to a normal E.S.R.

H. A. Burt.

Ineffective Use of Streptomycin in Rheumatoid Arthritis. RICE, R. M., BROWNING, J. S., and POWELL, H. M. (1947). *Amer. J. med. Sci.*, **214**, 64.

The authors produced experimental proliferative arthritis in rats by the intravenous injection of a culture of a pleuropneumonia-like organism obtained from a spontaneous joint infection in a laboratory rat. Such lesions have been employed by various workers for the experimental study of rheumatoid arthritis. The present authors compared the therapeutic value of " myocrisin " and streptomycin on such material. Streptomycin was found to be of greater value, although the effectiveness of myochrysine was also confirmed.

For clinical trials 1 male and 8 female adult patients were selected, each suffering from moderately severe rheumatoid arthritis with raised erythrocyte sedimentation rate. Five patients were given 10 g. streptomycin in 5 or 6 days, in 200 to 250 mg. doses injected intramuscularly 3-hourly; 1 patient was given 4 g. daily for 20 days, and 3 patients 4 g. daily for a week all in the same dosage 3-hourly, 2 of the last 3 having further small doses for 1 or 2 days later. Drug reaction limited treatment in these 2 patients. " In no case was there definite evidence of objective improvement. As is so often true with new remedies for arthritis, subjective improvement was quite general, and 3 patients claimed definite benefit for as long as 4 or 5 months following completion of treatment. It is interesting to note that those receiving the greatest amount of streptomycin seemed to improve the least. The erythrocyte sedimentation rate was not altered significantly by streptomycin." Drug reactions were common, and included nausea, fever, rashes, and deafness with vertigo.

[Two points are brought out by this paper: pleuropneumonia polyarthritis in rats does not react to all drugs in a similar manner to human rheumatoid arthritis, and streptomycin is unlikely to be of much benefit in rheumatoid arthritis in man.] *G. I. C. Ingram.*

Treatment of Rheumatoid Arthritis. Results with a New Gold Compound of Low Toxicity. ROSE, P. A. (1947). *Illinois med. J.*, **92**, 175.

Aurothioglycolanalide (" lauron ") is a new gold salt, prepared as a suspension in sesame oil. It contains 54·3% of gold, and is insoluble in water and organic solvents. A clinical trial of its value in 91 cases of rheumatoid arthritis is described, and the author appears favourably impressed.

He states that gold salts offer the best hope of bringing about clinical improvement, but owing to the high incidence of toxic reactions there is a reluctance to employ this form of treatment. In his series of 91 cases, treated with this new salt and controlled by the usual haematological and urinary investigations, he noted marked improvement in 73% and moderate improvement in a further 11%, with a follow-up period of about 1 year. The dose used was increased from 10 mg. to 100 or 150 mg. given twice weekly, with a maximum dose of 5 g. in any one course. This dosage tended to result in local joint reactions, after which clinical improvement was usually noted. Reactions were limited to mild nausea and vomiting, and in 11 cases non-progressive skin rashes occurred.

[On modern standards dosage was very high; most workers now limit total dosage in any one course to 1 g. of " myocrisin " or " aurocalcium ", and in such dosage results appear comparable with those in the present series, with minimal toxicity. In a larger series this new drug might well produce toxicity in such high dosage. This article does not evaluate any further the ultimate position of chrysotherapy in rheumatoid arthritis.] *D. P. Nicholson.*

BAL in the Treatment of Toxicity from Gold. MARGOLIS, H. M., and CAPLAN, P. S. (1947). *Ann. intern. Med.*, **27**, 353.

Toxic reactions from gold given in the usual therapeutic doses for rheumatoid arthritis include a severe form of stomatitis, mild conjunctivitis, anal ulceration, and dermatitis. BAL will probably be found to be a valuable antidote, especially if given early. It has proved of value in the treatment of arsenical and mercurial

poisoning, in clinical practice, because of its power to combine with the toxic metal before the latter can be lodged in the tissues.

The present paper is a short review of the use of BAL in 5 cases of toxic reaction to gold; 0·15 g. of BAL was given intramuscularly four times daily for 2 days and thereafter twice daily. The general plan was to give 2·5 g. in equal doses over 8 days. Unpleasant soreness at the site of injection and some nausea were reported, but improvement attributable to BAL was seen in 4 of the 5 cases; it was very striking in 2 of them.

G. F. Walker.

Treatment of Chronic Rheumatism by Organic Salts of Copper. (Le traitement des rhumatismes chroniques par les sels organiques de cuivre.) FORESTIER, J., and CERTONCINY, A. (1947). *Rev. Rhum.*, **14**, 271.

This article on work already recorded (*Presse Méd.*, 1946, **54**, 884; see abstract p. 256 in the *Annals* for December, 1947) analyses results of treatment by intravenous injection of an organic salt of copper in 50 cases of chronic rheumatism, of which 36 were arthritis of rheumatoid type. All received two or more series of injections, except 1 who made a remarkably complete recovery with one series. This was a man aged 35, incapacitated by active polyarthritis with constitutional disturbance. A total of 2·5 g. of the copper compound was given in bi-weekly intravenous injections each of 0·25 g. Joint pains and effusions began to diminish after the first few injections, and in 3 weeks he was up and about. After 2 months he appeared completely restored to normal health, with no signs of joint changes; the erythrocyte sedimentation rate (E.S.R.) had fallen from 80 mm. in 1 hour to 4 mm. in 1 hour.

Details are given of the treatment in patients who had shown either resistance or intolerance to gold therapy. For example, a woman aged 42 years had suffered from chronic progressive polyarthritis for 10 years. She had received two courses of gold injections each year from 1935 to 1939, without toxic reactions but with a poor therapeutic result. She was given nine series of copper injections and a total of 26 g. of the compound. Improvement came slowly, but was marked; joint swellings diminished and walking became possible again; the E.S.R. fell from 115 to 45. In another case, a woman aged 40 years, suffering from a severe and extensive form of rheumatoid arthritis, had had toxic reactions in the skin and mucous membranes from gold therapy. She was given copper injections, at first ten injections of 0·1 g., then ten of 0·25 g. Treatment was continued for 4 years or more, nine series in all being given and a total of 17 g. of the copper compound. Improvement was only slight during the first three series, but after this she improved progressively, until she was finally free from joint swellings and leading a normal life.

Kenneth Stone.

The Use of Folic Acid in the Treatment of Anemia of Rheumatoid Arthritis—A Preliminary Report. STEPHENS, C. A. L., BORDEN, A. L., HOLBROOK, W. P., and HILL, D. F. (1947). *Ann. intern. Med.*, **27**, 420.

A constant feature of rheumatoid arthritis is a moderate degree of anaemia of the hypochromic microcytic type which on careful study will nearly always be found to be singularly unresponsive to all the usual anti-anaemic agents. Folic acid in doses of 20 mg. daily will bring about a general improvement in the blood picture of most patients suffering from anaemia in rheumatoid arthritis, but no case should be regarded as unresponsive until a very much larger dosage, say 100 g. daily, has been gradually attained, since requirements vary. Administration of iron is no advantage. The main features of rheumatoid arthritis are not in any way improved by folic acid administration, but, on the other hand, there are no deleterious or toxic effects from the drug. Its influence on haematopoiesis, at least in rheumatoid arthritis, is clearly different from that of liver or iron.

G. F. Walker.

The Neuromuscular System in Rheumatoid Arthritis. Electromyographic and Histologic Observations. MORRISON, L. R., SHORT, C. L., LUDWIG, A. O., and SCHWAB, R. S. (1947). *Amer. J. med. Sci.*, **214**, 33.

Muscle weakness, usually associated with atrophy, constitutes one of the most disabling features of rheumatoid arthritis. Early in the disease, motor weakness, often accompanied by numbness and paraesthesiae, may strongly suggest the diagnosis of primary neurological disorder.

In patients with rheumatoid arthritis electromyographic tracings showed some involuntary activity of muscle in relation to diseased joints which was apparent neither to patient nor to observer. In 1 patient such disordered muscle function appeared to precede any clinical evidence of articular disease in the region. This spontaneous muscular activity is not peculiar to rheumatoid arthritis; it was found in 2 out of 4 patients with arthritis due to acute specific infections and in one with joint disability due to fixation. A closely similar pattern may be seen in anterior poliomyelitis, infective polyneuritis, and in nerve injuries. The authors have shown in cases of rheumatoid arthritis that blockage of the peripheral nerve is capable of interrupting the path of origin of these motor discharges. Electromyographic evidence of upper motor neurone involvement could not be demonstrated.

In 44 patients with rheumatoid arthritis the central nervous system showed no specific lesions post mortem, but changes in the lateral projections of the anterior horns, usually attributed to ageing, were more pronounced than in a control group of similar age distribution. In a proportion of cases non-specific inflammatory lesions, similar to those reported by other observers, were found in the peripheral nerves and in the muscles.

It is concluded that rheumatoid arthritis causes direct involvement of the neuromuscular system, and that spontaneous skeletal muscle activity may be caused by pathological lesions in the lower motor neurones.

T. Semple.

Progressive Chronic Polyarthritis. (La Polyarthrite Chronique Progressive.) MICHOTTE, — (1947). *Arch. Rhum.*, **7**, 41.

Since the author's first reports in 1942 on rheumatoid arthritis (for which he uses the name chronic progressive polyarthritis, C.P.P.), Kersley's book "The Rheumatic Diseases" (1945) and Costes' and Gaucher's reports on chronic progressive rheumatisms of inflammatory origin (1946) have been published, and their views differ in certain points with those of the present author. The study of records of 250 cases of rheumatoid arthritis leads him to the opinion that under the collective name of C.P.P. three different diseases can be differentiated: (1) The authentic C.P.P.; (2) destructive polyarthritis; (3) exudative polyarthritis.

(1) Chronic progressive polyarthritis begins with

indefinite arthralgias accompanied by some constitutional upset. The affected joints, mainly hands, show fusiform swelling with atrophy of muscles and, later, of epiphyses; the skin over the joints is cold and clammy. It finally results in deformities of the affected joints and their ankylosis. The disease is steadily and inexorably progressive and defies all treatment. *X*-ray examination shows the characteristic band of decalcification across all the fingers of the affected hand and a rotation of the metacarpal heads towards the ulnar border. The erythrocyte sedimentation rate (E.S.R.) is moderately raised and the blood shows a slight anaemia (3·75–3·25 mil.) with a normal colour index and some leucopenia with relative lymphocytosis.

(2) In destructive polyarthritis a characteristic destruction of cartilage and underlying bone occurs, followed by osseous ankylosis. The disease begins in one or two joints which do not show much atrophy. The skin of the affected parts is not cold or clammy. There is no constitutional upset and no pyrexia. Frequent remissions are followed by exacerbations, but spontaneous arrest of the disease sometimes occurs. In this form chrysotherapy is most effective. On *x*-ray examination punched out areas of rarefaction in the affected bone with subsequent destruction of the articular cartilage is shown. The E.S.R. is very high, and flocculation of the red cells at the level of the packed cells is considered a characteristic sign. Normocytic anaemia with moderate leucocytosis completes the picture.

(3) Exudative polyarthritis is a disease of women in the fifth decade. The first joints affected are the metacarpo-phalangeal followed by the large joints of the body, such as knees and wrists. Exudation into the joints is followed by swelling, but there is remarkably little pain. A ground-glass appearance of the affected bones on *x*-ray examination is characteristic. There is no obvious general upset.

In conclusion the author disagrees with Kersley that his two forms of rheumatoid arthritis, the primary rheumatoid, atrophic type, and the secondary rheumatoid, focal type, are explained aetiologically, the former being the response of the soil to the seed, the latter representing the original focus of the disease. He was able to differentiate these three distinct diseases without attaching an aetiological significance to any of them.

J. Koszyk.

Chronic Progressive Osteolytic Polyarthritis. (La polyarthrite chronique evolutive osteolytique.) JUSTIN-BESANÇON, L., RUBENS-DUVAL, A., and DUCHE, D. J. (1947). *Rev. Rhum.*, **14**, 353.

The Mester Test in the Differential Diagnosis between Scarlatinal Rheumatism and Rheumatic Polyarthritis. (La prova di Mester quale elemento diagnostico differenziale tra la reumatoide scarlattinosa e la poliartrite reumatica.) CARTAGENOVA, L. (1947). *Policlin infant.*, **15**, 475.

This article reports unsatisfactory results of the test in the two conditions cited.

Some Practical Considerations in the Management of Arthritis. HOLLANDER, J. L. (1948). *W. Va. med. J.*, **44**, 1.

Surgical Treatment of Chronic Arthritis of the Hip. (A propos du traitement chirurgical des arthrites chroniques de la hanche.) TRÈVES, A. (1947). *Rev. Rhum.*, **14**, 374.

(Osteo-Arthritis)

Arthrodesis of the Hip Joint in Degenerative Arthritis. A Modified One-stage Procedure with Internal Fixation. DICKSON, J. A., and WILLIEN, L. J. (1947). *J. Bone Jt. Surg.*, **29**, 687.

A one-stage operation is described for arthrodesis of the hip. The joint is approached through a Smith-Petersen incision, but is not dislocated. The cartilage lining the acetabulum and the femoral head is thoroughly fragmented *in situ* by a chisel, after which any deformity present can readily be corrected. Then, through a separate lateral incision a triflanged nail is driven up the neck through the head and into the acetabulum. After insertion of the nail the joint is impacted. Finally, a graft from the ilium is laid along the upper surface of the raw neck of the femur and slotted into the acetabulum. No external fixation is used. The patient lies free in bed; within a few days he is rolled over into the prone position and active knee flexion is encouraged. He is allowed up on crutches in 4 to 6 weeks. There was fusion in all 10 patients and no recurrence of deformity.

George Perkins.

(Spondylitis)

Ankylosing (Marie-Strümpell) Spondylitis. (An Analysis of 100 Cases.) GRAHAM, W., and OGRYZLO, M. A. (1947). *Canad. med. Ass. J.*, **57**, 16.

The clinical and diagnostic features of ankylosing spondylitis are described. Out of 850 rheumatic patients admitted in 2 years to a Canadian Service Arthritic Unit, 100 suffered from spondylitis. The ratio of spondylitis to rheumatoid arthritis was 1 in 2·8. An average of 5·7 years elapsed from the time of onset of symptoms to recognition of the disease. In 27% of the cases there was peripheral joint involvement, in some cases multiple. It is surprising to note that the knees were involved in 22%, whereas the hips were involved in only 10% and the shoulders in only 4%. In all cases associated with urethral infection the peripheral joints were affected before those of the spine. As the authors point out, the frequency with which the onset of the disease is peripheral emphasizes the need for careful spinal examination in all cases of rheumatoid arthritis, otherwise latent involvement of the spine may be overlooked.

H. A. Burt.

Initial Symptoms of Spondylitis Ankylopoietica. (Initialsymptomer ved Bechterews sykdom (Spondylarthritis ankylopoietica)). TANBERG, A. (1947). *Tidsskr. norske Laegeforen*, **67**, 192.

The symptoms which, in the author's opinion, should arouse suspicion of an early spondylitis are: pain in the back, especially at night, iritis, increased erythrocyte sedimentation rate (E.S.R.), periostitis with varying localization, joint pains especially in hips and shoulders, and changes in the sacro-iliac joints. In the early stages the patient often complains of a tired feeling across the sacral region. The pain is seldom referred to the sacro-iliac joints, in contradistinction to a tuberculous lesion of one of these joints where the patient points to one of them as the seat of the pain. The pain is often felt in the gluteal region or the inner side of the thighs or groins, or it may present the picture of sciatica. Sometimes it is felt higher up and may radiate forward like an intercostal neuralgia. As a rule it is worse at night or in the early morning. These severe pains, which make the

patient get out of bed during the night, are often insignificant or absent during the day. The author regards these pains as diagnostic if they are associated with an increased E.S.R. Iritis is well known as a complication of chronic polyarthritis but is much more common in spondylitis ankylopoietica. The incidence of iritis in polyarthritis is about 4 to 5% whereas it may be as high as 20% in spondylitis. As a rule the E.S.R. is raised. It may be as high as 100. On the other hand, it may be normal.

The author mentions a number of peculiar symptoms and signs, which he associates with lesions in the periosteum or tendon attachments and which, he maintains, are present in every case of spondylitis ankylopoietica. The areas most commonly affected are: under the heel and over the ischial tuberosity and iliac crest. A tender point is often found 2 to 3 in. (5 to 7·5 cm.) behind the anterior superior iliac spine. Joint symptoms outside the spinal column are very common. Involvement of the hips and shoulders is typical. The author attaches diagnostic value to involvement of the sterno-clavicular joint, but he does not attach any great importance to gonorrhoea or urethritis as aetiological factors.

Radiographs of the sacro-iliac joints confirm the diagnosis, though it may be necessary to repeat the examination at intervals over a long period.

C. C. Holm.

Degenerative Bone Disease. Findings in 18 Cases with Posterior Spurs of the Lumbar Vertebrae. SOLOMON, W. M. (1947). *Amer. J. med. Sci.*, **214**, 163.

The presence of spurs or osteophytes on the posterior aspects of the bodies of the lumbar vertebrae has not received much attention and few references are available. The author examined 910 spines radiologically, the lumbo-sacral region being examined in 629. Eighteen of the latter showed spurs arising from the posterior surfaces of the bodies of the vertebrae. The average age of these 18 patients was 33 years, range 21 to 39 years. Two-thirds of the patients recalled an acute injury to their backs which required rest in bed or cessation from work. The time between the injury and admission to hospital varied from 3 months to 25 years, with an average of 6 years. The symptoms in the lower back varied from mild discomfort to severe disabling pain. In 2 the complaints were typical of osteo-arthritis—namely, dull aching aggravated by changes in position and weather. The other 16 patients had symptoms similar to the herniated disc syndrome, with pain worse at night and on coughing or sneezing, with a history of partial or complete remission between attacks, and radiation of pain down the posterior part of the leg to the foot or down the lateral and medial aspects of the thigh. Twelve patients showed loss of the normal lumbar curve, spasm and tenderness of the lumbar muscles, and a positive straight leg-raising sign. The ankle-jerk was absent in 3 and paraesthesiae were present in 1. The blood count, sedimentation rate, and cerebrospinal fluid were normal, and the blood test for syphilis was negative.

Many investigators believe that degenerative changes in the spine are the result of lesions in the vertebral discs, and reference is made to experimental work in which, 3 months after posterior injury of the disc in dogs, a marked hyperostosis appeared. Unfortunately, because of the exigencies of military service, the 18 patients in the author's series could not be followed up sufficiently to prove the relation of spurs to symptoms. They are reported so that further observations may be encouraged.

S. Oram.

Changes in the Intervertebral Disk and Articulations in Brucellosis. (Las alteraciones del disco y de las articulaciones intervertebrales en la brucelosis.) DE VILLAFANE LASTRA, T. (1947). *Rev. méd. Cordoba*, **35**, 319.

The author describes 7 cases of brucellosis in all of which there was affection of the vertebral column. In the radiological pictures the lesions of the intervertebral disc, with or without a hernia of the nucleus pulposus, and the spondylitic changes in the lumbar vertebra, which sometimes led to a complete destruction of the vertebral body, were visible. In some patients the hernia of the intervertebral disc produced a compression of the spinal cord, with the clinical features of local or root symptoms or a meningo-myelitis. Other cases showed changes in the intervertebral articulations and the spinous process causing osteo-arthritis.

[The importance of the paper lies in the fact that the author was able to show the aetiological connexion between brucellosis and pathological changes in the vertebral column, which even the most recent British textbooks fail to mention.] *Franz Heimann.*

A Rare Affection of the Spinal Column Simulating Spondylosis Rhizomelica on Physical Examination. (Een zeldzame afwijking van de wervelkolom, bij physisch onderzoek het beeld gevend van spondylosis rhizomelica.) VAN DAM, G., and STEINER, F. J. F. (1947). *Ned. Tijdschr. Geneesk.*, **91**, 1546.

A case in which physical examination pointed to spondylosis rhizomelica, whilst *x*-ray examination showed almost exclusively narrowed intervertebral discs, is presumed to be due to so-called fibrosis of the intervertebral discs, a syndrome described by Schmorl and Güntz.—[Authors' summary.]

Two Cases of Ankylosing Spondytilitis treated with Penicillin. (Deux cas de spondylose rhizomélique traites par la pénicilline.) RUELLE, M. (1947). *Acta physiother. rheum. belg.*, **2**, 164.

Early Diagnosis of Spondylitis Ankylopoietica. (Zur Fruhdiagnose der spondylarthritis ankylopoetica.) VOLHARD, E. (1948). *Dtsch. med. Wschr.*, **73**, 111.

Early Diagnosis of Spondylitis Ankylopoietica. (De vroege diagnose van spondylarthritis ankylopoetica (Ziekte van Bechterew).) GOSLINGS, J. (1948). *Ned. Tijdschr. Geneesk.*, **92**, 627.

Gout

The Nature of the Deposit in Gouty Tophi. (Zur Frage der Natur der Ablagerungen in den Gichtknoten.) BRANDENBERGER, E., DE QUERVAIN, F., and SCHINZ, H. R. (1947). *Schweiz. med. Wschr.*, **77**, 642.

Examination of a tophus from a case of gout by *x*-ray crystallography showed it to contain microcrystals of sodium monourate hydrate [$Na(C_5H_3O_3N_4).H_2O$]. No other crystalline or amorphous substance was identified. *S. S. B. Gilder.*

Diagnosis and Management of Gout. LINDLEY, E. L., and MIDDLETON, J. W. (1947). *Tex. St. J. Med.*, **43**, 530.

Gout: A Review of Diagnosis and Management. HAGEMANN, P. O. (1948). *J. Mo. med. Ass.*, **45**, 192.

Non-Articular Rheumatism

The Aetiology, Diagnosis, and Treatment of Prolapsed Intervertebral Disk, with a Review of 300 Cases of Sciatica. KENDALL, D. (1947). *Quart. J. Med.*, **16**, 157.

Cases of sciatica fall into certain diagnostic groups: (a) intervertebral disc protrusions; (b) inflammation or disease of muscular or fascial structures; (c) involvement of the cauda equina, sacral plexus, or sciatic nerve by gross disease of neighbouring structures; (d) cases having a functional basis.

In the patients with disc protrusion, trauma was the important factor, while in myofascial sciatica exposure to cold and rheumatic predisposition played a more important part. A single relatively severe injury, such as a fall from varying heights with the spine flexed, was common in disc injuries, while repeated minor injuries often took the form of lifting heavy weights in circumstances of mechanical disadvantage. Two cases followed lumbar puncture which had been performed with great difficulty. Congenital abnormalities of the lumbar spine, excluding spondylolisthesis, were found in approximately 12% of patients, but a similar proportion was found in a control group. Although exposure to cold and damp does not play a prominent part in the production of the initial symptoms of a prolapsed disc, a recurrence of the symptoms is not infrequently precipitated in this way.

The syndrome of the typical prolapsed disc consists of three main phases: initial trauma, a history of which was present in 86%; onset of pain in the back, immediate in 72%; and later onset of pain in the leg or true sciatic pain. The initial pain is usually referred to the midline of the lumbar region, with a tendency to spread laterally or into the buttocks or thighs. It is rare for the pain to extend into the calf or foot at this time. The pain varies greatly in severity both in the same patient and from case to case. This "muscle spasm" phase is self-limiting and independent of treatment, usually lasting for 2 to 3 weeks. Attacks of this kind, perhaps after trivial trauma or exposure, may be repeated over a period of years before the appearance of pain in the leg, which was the initial symptom, however, in 40% of the patients. This pain in the leg may also be subject to remission, either spontaneously or as a result of rest. It is often of two distinct types: the pain in the buttock and thigh is a dull gnawing or aching sensation, whereas that in the leg and foot is described as a sharp stab, a painful numb feeling, or a burning sensation, and is more subject to alteration by movement or exertion—it has in fact many of the features of true root pain.

Physical signs fall into two main categories: (1) those primarily mechanical and due to changes in ligamentous and fascial structures in the lumbar region, such as alteration in the normal lumbar curve, spasm of the erector spinae muscles, scoliosis and disturbances of active and passive spinal flexion and extension; (2) neurological signs, due to pressure on the nerve root by the disc protrusion, and consisting of local tenderness, Lasègue's sign, and motor, sensory, and reflex disturbances. No motor weakness of the muscles was demonstrated, but a well-marked hypotonia of the calf muscles with wasting was a common finding. No constant relation between the area of sensory disturbance and the site of disc protrusion was demonstrable; a protrusion between the fifth lumbar vertebra and the sacrum was never associated with a sensory disturbance in the fifth lumbar distribution. Diminution or loss of ankle-jerk was present in 63% of patients, and of knee-jerk in only 2·5%. Motor, sensory, and reflex disturbances, once present, tend to persist during remissions and may do so after laminectomy. The cerebrospinal fluid is usually normal. The history and physical signs of prolapsed disc are sufficiently definite to justify a diagnosis without the use of contrast-medium radiography.

Differentiation of the early case of disc prolapse from a purely "fibrositic" condition may be very difficult and may rest largely upon negative findings in the latter condition. The procaine injection test is of some help in this connexion; in myofascial referred pain, procaine injection into the painful area abolishes temporarily, and occasionally permanently, both symptoms and signs.

The essential treatment of sciatica is rest in bed, with graduated exercises later. There is every reason to believe that it is a self-limiting condition; for this reason caution should be exercised in recommending surgery. In the present series 92 patients were submitted to operation for removal of disc protrusion, and 64 of these obtained immediate relief from symptoms. At best, operation is only a short-cut in an otherwise tediously protracted disease.

[This important article should be read in full.—Ed.]

T. Semple.

Value of the Location of Valleix's Points in the Topographical Diagnosis of Sciaticas due to Disk Lesions. (Intérêt de la recherche des "points de valleix" pour le diagnostic topographique des sciatiques d'origine discale.) DE SÈZE, S., CHEVROLLE, J., and DENIS, A. (1947). *Rev. Rhum.*, **14**, 123.

Disc lesions may be located from clinical signs only, without the help of "lipiodol". The condition of the ankle-jerk, the site of the spontaneous pain, the presence of hypoaesthesia, and the radiation of the pain produced by pressure on the vertebrae have value in location. The pain provoked by pressure on the space L4–L5 or L5–S1, either between or lateral to the vertebrae, corresponds to a lesion of the corresponding intervening disc. Pressure over Valleix's points also gives useful information. When the fifth lumbar root is involved the usual painful points are in the outer part of the buttock, outer parts of the back of the thigh, popliteal space, and back of the leg (less commonly the lateral aspect of the leg, or even over the peroneal muscles), and over the external malleolus or the pre-malleolar groove. When the first sacral root is involved the points are on the inner part of the buttock, and the medial parts of the back of the thigh, popliteal space, and leg. Pressure on the tendo Achillis often produces pain in the ankle and heel even when the spontaneous pain does not descend to this level. The value of these observations has been confirmed in 41 cases; the fifth lumbar root was affected in 16 and the first sacral in 25.

J. G. Reah.

Variations in the Syndrome of the Ruptured Intervertebral Disc in the Lumbar Region. KRISTOFF, F. V., and ODOM, G. L. (1947). *Surgery*, **22**, 83.

This paper describes a number of variations that may occur in cases of ruptured intervertebral disc and in the associated syndromes. Low back pain is the outstanding complaint in all cases. Sciatic pain may be felt on one or both sides or not at all. A symptom of much value in indicating rupture of the disc in the higher lumbar interspaces is radicular pain. A protrusion that occurs otherwise than laterally or which is large enough will always affect several roots. Myelography is recommended in cases in which clinical location of the rupture is not possible.

A. M. A. Moore.

Herniated Intervertebral Disk. Analysis of Ninety Cases. PEYTON, W. T., and SIMMONS, D. R. (1947). *Arch. Surg., Chicago*, **55**, 271.

The results of operation for herniation of an intervertebral disc in 90 patients have been analysed. The diagnosis of a disc lesion was verified by finding either an extruded loose fragment of disc tissue or a definite bulging of the disc with spontaneous protrusion of nuclear material when the annulus fibrosus was incised. Eighty cases came into one or other of these categories. In some of the patients operated upon not only was nuclear material removed from the disc but spinal fusion was performed as well. Seventy-two of these 80 patients were studied later and only 3 had continual pain or disability. The remainder were regarded as in a satisfactory condition. In 10 patients, whose disc at the time of operation did not fulfil the criteria referred to above, the results were not good. The authors conclude that simple removal of the nuclear material is satisfactory if there is an undoubted disc lesion, and that improvement in results is more likely to be obtained through a better selection of cases for operation than through the introduction of any new operative procedures.

Lambert Rogers.

Fibrositis (Muscular Rheumatism) including Dupuytren's Contracture: A New Method of Treatment. STEINBERG, C. L. (1947). *N. Y. St. J. Med.*, **47**, 1679.

This paper defines the author's general conception of primary fibrositis. He takes the middle road between those who state that there is no such condition and those whose "liberality was recently reached . . . when herniation of fat through a tear in the fascia of the back was labelled fibrositis". The general picture drawn of the condition conforms with that usually accepted [although there may be those who could not subscribe to the statement that "Dupuytren's contracture is a form of primary fibrositis"].

The author mentions a previous report that creatinuria is an important and significant finding in primary non-psychogenic fibrositis. Excretion of up to 136 mg. in 24 hours is normal in male adults; 150 mg. in 24 hours is always found in primary fibrositis, and the figure is usually between 300 and 400 mg. A similar creatinuria is seen in the experimental laboratory animal on a diet deficient in vitamin E. The creatinuria is generally relieved by an adequate vitamin-E intake. The vitamin-E level in the blood can be estimated by the method of Quaife and Harris (*J. biol. Chem.*, 1944, **156**, 499) and has been shown to be low in some cases of fibrositis. The author inclines to the hypothesis that although in some instances there may be a nutritionally deficient intake or absorption of vitamin E by reason of hepatic damage in fibrositis, there is primarily a deficiency in the utilization of tocopherols by muscle.

The author's treatment consists of administration of 300 mg. mixed natural tocopherols, of which 60% is in the form of α-tocopherol, in equally divided doses per day. A maintenance dose of 1 mg. per kilo body weight is required later for several months after cessation of symptoms. Occasionally a higher maintenance dose is needed, up to 300 mg. a day. Objective evidence of improvement is mainly noted in Dupuytren's contracture. Clinical cure of a contracture present for 1 year was achieved in 4 weeks, and there was considerable improvement in a case of 30 years' standing with 9 months' treatment. Several individual cases of satisfactory improvement are referred to, but no numerical summary of cases so treated is included.

Harry Coke.

Scapulo - Humeral Periarthritis. (Les periarthrites Scapulo-humérales.) RUELLE, M. (1947). *Arch. Rhum.*, **7**, 54.

Scapulo-humeral periarthritis (S.H.P.) comprises every painful rigidity of the shoulder caused by involvement of the periarticular tissues. A marked increase of S.H.P. after the war is noted. The increase is due mainly to forms where single tendons were involved: actual partial periarthritis. The high incidence in the fifth decade is due aetiologically to progressive circulatory improverishment of the connective tissue of the joint. This circulatory disturbance originates often in irritative states of the sympathetic system. The author quite frequently found a cardio-aortic source of the irritation passing through C4, C5, C6, to the shoulder. Other causes are injuries to the shoulder, action of cold, and arthritic states in the cervical spine. Treatment should be adapted to the various forms of S.H.P. Acute forms may require blocking of the stellate ganglion or radiotherapy to the cervical sympathetic ganglia. *J. Koszyk.*

Notes on Some Common Forms of Non-Articular Rheumatism. (A propos de quelques formes courantes de rhumatisme abarticulaire.) CORNIL, M. (1947). *Arch. Rhum.*, **7**, 61.

An account of manifestations of non-articular rheumatism of the neck, shoulders, and upper limb is given. The periarticular tissues can be affected by rheumatic processes as well as the articulations themselves. Cervico-brachial neuralgiae and neuro-myalgiae, torticollis, subacromial and subdeltoid bursitis, epicondylitis of the elbow, various tendo-synovitides of the wrist, and Dupuytren's contracture of the hands are all discussed. Frequently a masked spondylosis of the cervical spine is the source of the symptoms, and lesions of the spine are at the root of one third of cases, mainly of C5 and C6. Other aetiological factors, like trauma, infection, and neurotrophic troubles, are also discussed. Lériche's view of the paramount importance of minor trauma to the sympathetic system which cause vasomotor disturbances in rheumatic conditions of the affected tissues is supported. Full investigation of the sympathetic system should be carried out in all such cases. The treatment of every manifestation is described, and its specific indications given. In the treatment of Dupuytren's contracture no convincing results were obtained with parathyroid extract, and surgical treatment is advocated. [The author is obviously unaware of the newest views on this subject.]

J. Koszyk.

End-Result Study of the Intervertebral Disc. LENHARD, R. E. (1947). *J. Bone Jt. Surg.*, **29**, 425.

Advantage of the "Anterior Film" Technique in Radiography of the Lumbo-sacral Junction in the Erect Position. Application of the Method to the Study of Scolioses with Pelvic Imbalance. (Sur les avantages d'une technique "ampoule dorsale—film ventral" pour la radiographie de face de la charnière lombo-sacrée en position de bout. Intérêt de cette méthode pour l'étude des scolioses avec déséquilibre pelvien). DE SÈZE, S., and COLIEZ, R. (1947). *Rev. Rhum.*, **14**, 370.

Origin of Pain in Sacralization: Importance of the Hinge-Disk (L4–L5). (Origine des douleurs dans la sacralisation douloureuse importance des altérations du Disque Charnière). DE SÈZE, S., and SALOFF, J. (1947). *Rev. Rhum.*, **14**, 368.

General Articles

The Appearance of Acute Phase Protein in Various Diseases. [In English.] HEDLUND, P. (1947). *Acta med. scand.*, Suppl. 196, 579.

The presence of acute phase protein was investigated in about 2,000 general medical cases. The technique was that of the Neufeld reaction: one drop each of pneumococcus type 27 suspension, patient's serum, and methylene blue were mixed on a slide, the reaction being read after a few minutes. Pneumococcus suspensions of varying densities were used. The least dense suspension—No. 1—had 2 to 4 organisms per microscopic field, and sera which reacted only with such a suspension were said to have acute-phase protein in titre +1. Sera of titre +2 reacted with a suspension containing twice as many organisms as in suspension No. 1, while suspension No. 4 had double the number of organisms as suspension No. 2, No. 8 double that of No. 4, and so on. Suspension No. 16 had a density of about 1,000 million organisms per ml.

In rheumatic fever, all of 21 cases investigated had acute-phase protein. In rheumatoid arthritis, 94 out of 128 cases gave positive results. These cases were in the acute stage. *R. B. Lucas.*

Rheumatic Pneumonitis. A Case of Widespread Chronic (Proliferative) Type with Acute (Exudative) Foci. MUIRHEAD, E. E., and HALEY, A. E. (1947). *Arch. intern. Med.*, **80**, 328.

A review of the literature reveals that, although there is general agreement on their morphology, a difference of opinion exists regarding the precise pathogenesis and the specificity of the pulmonary lesions which for many years have been known to occur during the course of rheumatic fever. As evidence that the changes in the lungs have a definite rheumatic basis, the authors report a case in which both healed and active cardiac lesions were accompanied by widespread interstitial and intra-alveolar pneumonitis. The patient was a woman, aged 25, with the classical picture of mitral stenosis and repeated bouts of congestive heart failure. The diagnosis of rheumatic pneumonitis was first considered when *x*-ray examination 6 weeks before death showed a confluent pneumonic consolidation at the right base; subsequently signs of consolidation developed in the right middle and lower lobes. At necropsy the heart showed the typical appearance of active and healed rheumatic disease, with pronounced mitral stenosis. The changes in the lungs were not uniform: the upper lobes were dark red, firm, and filled with frothy fluid; the lower lobes were firm, rubbery, and yellowish-grey, with a dry cut surface. Microscopically there was generalized thickening of the alveolar walls, due in the upper lobes to a capillary hyperaemia and increased cellularity; and in the lower lobes to abundant connective tissue. In the latter the lumen of the larger blood vessels was replaced by connective tissue in which there were scattered small blood vessels, giving the appearance of canalized thrombi.

In general, the pulmonary lesions conformed with those described by previous observers, but the authors point out that the haemorrhages, young connective tissue, proliferating fibroblasts, and cellular exudate found in the upper lobes suggested the presence of an active exudative phase of the rheumatic process in those lobes co-existent with a healed proliferative phase, with extensive fibrosis, in the lower lobes. *W. E. Hunt.*

Scarlatinal Rheumatism and Rheumatic Polyarthritis. (Il reumatismo scarlattinoso e la poliartrite reumatica.) CARTAGENOVA, L. (1947). *Policlin. infant.*, **15**, 369.

In a series of 560 cases of scarlet fever, there were 21 cases of early rheumatism (first or second week) and 7 of late rheumatism (fifth or sixth week). The cases of early rheumatism were benign, without cardiac involvement or radiological signs and chiefly involving small joints. The E.S.R. was only slightly raised. The late cases on the other hand, were severe, involved large joints, and in 5 cases led to chronic cardiac disability. The E.S.R. was invariably much higher than in early cases. Mester's test was of no diagnostic value. The early cases are regarded as scarlatinal and the late as manifestations of acute rheumatism. *S. S. B. Gilder.*

Bornholm Disease in the Tropics. JAMIESON, W. M., and PRINSLEY, D. M. (1947). *Brit. med. J.*, **2**, 47.

Bornholm disease has a number of synonyms, mostly descriptive, such as " epidemic myalgia ", " devil's grip ", " epidemic myositis ", and " acute benign dry pleurisy ". Outbreaks have been reported from Northern Europe, U.S.A., Britain, Southern Australia, and Egypt; 35 cases were seen in Aden between Aug. 17, and Oct. 25, 1946, and with 1 exception were confined to Service personnel and their families.

The onset was abrupt, with pain, headache, and some fever as the three commonest features. The pain was either sharp or of a constrictive nature, always made worse by respiratory effort; there was no position in which all patients felt most comfortable. Pain started in the epigastrium in 8 cases, along the right costal margin in 6, and along the left costal margin in 4. Pain was referred in 11 cases to shoulder-tip, interscapular region, or umbilicus to groin. It lasted usually from 3 to 7 days, once for as long as 23 days. Headache was present in 18 cases; often excruciating, it lasted up to 4 days, leaving the patient with a dull ache for several more days. There was fever at the onset in all cases except 1; the temperature was not usually above 100° F., but the highest reached was 105° F. Other symptoms complained of were sore throat, anorexia, nausea, vomiting, giddiness, and diarrhoea (the last being normally very common in Aden).

Examination of the chest revealed abnormality in 1 case only—a pleural rub lasting for 8 days. Tenderness was found in half the cases, mainly subcostal but in 3 cases it was epigastric. Radiographs taken in 25 cases showed the diaphragm to be freely mobile in all. Red-cell counts were normal, but white-cell counts varied from 8,000 to 13,000 per c.mm.; the erythrocyte sedimentation rate was also raised. Twelve out of 30 male patients had orchitis, which was the outstanding complication, starting after the eighth day and lasting from 2 to 6 days. Treatment was symptomatic; codeine, aspirin, and the barbiturates were useful, although morphine was sometimes necessary to relieve the severe headache.

Sporadic case of Bornholm disease need to be carefully distinguished from pleurisy, an upper abdominal surgical condition, and early infective hepatitis. Malaria gave rise to occasional difficulties. The causal agent is not known, though evidence points to a virus infection spread by droplets. Thus, Aden is within 24 hours by air from Egypt, which makes the introduction of infection easy, even where the incubation period is short. Moreover, an R.A.F. officer, his wife, and their 2

children all developed the disease within a period of 11 days, and there were several cases among the hospital staff. The authors do not think that infected water, milk, or food could be incriminated, or that insects were likely to have carried the organism. *T. E. C. Early.*

Decalcification in Rheumatology. (Les décalcifications en Rhumatologie.) FEROND, M. (1947). *Arch. Rhum.* 7, 60.

In acute and chronic rheumatic disease little attention is being paid to the state of calcium impregnation of the bones as shown by *x*-ray examination. A decalcification is very constant, but the underlying biochemical disturbances are unknown. Food restrictions in Belgium in the last war produced considerable decalcification of the bones and joints in individuals suffering from rheumatic disease. The response to treatment of the so-called great osteomalacias of famine was a striking feature; but in cases of chronic rheumatism treatment produced very little improvement of the Ca impregnation of the decalcified bone, although calcium blood levels were restored to normal. Radiographs showed very little improvement for long periods. Only further investigations of the biochemical processes of the tissues affected by disease can throw more light on this question.

J. Koszyk.

Osteo-articular Deficiency Diseases. (Maladies osteo-articulaires de carence.) JUSTIN-BESANÇON, L., and RUBENS-DUVAL, A. (1947). *Rev. Rhum.*, **14**, 197.

This is a clinical study of deficiency diseases of bone seen in France during enemy occupation and the role of privation in the causation of certain rheumatic diseases. Although rationing began in October, 1940, it was not until 1942 that some grave cases of famine osteomalacia appeared. In 1943 deficiency diseases of bone affected all classes of society and all ages, but predominantly females.

The diagnosis of famine osteomalacia in its severe form is simple, but recognition of the disease during the insidious onset is difficult and rests on a few clinical and radiological data. The therapeutic test is often the best criterion, for, while the disease shows no tendency to remission so long as privation lasts, it responds within some 3 weeks to calcium, phosphorus, and vitamin treatment. The presenting symptom is pain, deep, dull, and aching at first, in the interscapular or lumbar regions, pelvis, or lower limbs; later it is more violent and paroxysmal. Associated is an increasing muscular wasting and weakness, with some joint stiffness from muscular spasm. Radiological diagnosis, simple in the late stages when there are excessive bone transparency and thinning of the corticalis, must at the beginning often rest on a disappearance of the fine trabeculae of the spongiosa, which has a blurred or washed-out appearance. Laboratory tests such as can be carried out with the simpler facilities for investigation are not very helpful. Calcium and phosphorus levels in the blood may be within normal limits; there is a raised erythrocytes sedimentation rate; a slight elevation of plasma phosphatase offers suggestive evidence. Although the whole skeleton is affected, decalcification is often most marked in the spine or pelvis. Two groups are described: (1) generalized, with severe pain, cachexia, and muscular weakness; (2) localized. Most commonly the spine was affected, a condition often manifested by severe interscapular pain. Kyphoscoliosis may develop, and in severe cases there may be collapse of vertebral bodies. These cases were much more common in women than in men. Another form mainly affects the pelvis, and tends to be associated with pseudo-fractures (Milkman's syndrome).

Rations in France in 1941 provided only 10 and 25% of the normal daily requirements respectively of phosphorus and calcium; the diet was also deficient in vitamin D, estimated at 10 i.u. daily (whereas the daily need may be regarded as from 200 to 1,000 i.u.). Even now prophylactic measures in France would appear to be needed; it is suggested that milk consumption should be doubled, and a calcium bread like the English national loaf adopted.

Scapulo-humeral periarthritis became much more frequent during the occupation. The incidence of rhizomelic spondylitis also increased, being estimated to be in 1942 almost double that of pre-war years. The association of vitamin deficiency in these and other rheumatic disorders is discussed; but no clear evidence of causal relation is established. *Kenneth Stone.*

High Frequency Sound Vibrations in the Medical Treatment of Rheumatic Diseases. (Ultrasonórne chvenie v liečebnej praxi reumatických chorôb.) ZEMAN, J. (1947). *Bratislavské lekárs. List.*, 27, 449.

The author briefly discusses the main principles of the high-frequency sound vibration apparatus used in medical practice. The wave-length is an important factor regulating the quality and intensity of the high-frequency sound effect. This, again, depends on the nature and cutting of the crystal and also on the frequency, which itself depends on the connected oscillation cycle. No less important are the adjustment, and the intensity of the vibrations measured in watts.

Among the biological effects of high-frequency sound vibrations discussed are the mechanical twitching effect, cavitation, micromassage, and the thermal effect. The latter arises partly from the apparatus and partly in the body, depending on the resistance of the tissue concerned to the penetration of the vibrations. The liberated gases in the tissue are carbon dioxide and oxygen, but the amounts produced are insignificant. More importance is attributed to the liberation of the cell contents into the intercellular tissue spaces, where they act like a hormone with a local effect similar to that of protein shock therapy.

The author uses an apparatus with a vibration of 1,750 kHz, wave-length 7 mm., and a performance of 500 watts. The method used is a point application from various surfaces in order to obtain a maximal effect in the deeper layers of diseased tissue. Treatment consists of a total of 6 to 12 applications, combined with balneotherapy, and also some 20 applications without balneotherapy. Each session lasts 5, 10, 15, or 20 minutes, according to the response.

Treatment of 70 cases of diverse rheumatic conditions is reported. There was improvement in 46 and slight improvement in 20, but 4 cases of chronic sciatica became worse. The best results were obtained in early periarthritic ankylosis and fibrosis, chronic rheumatic swellings, and osteo-arthritis. Acute conditions of joints and nerves were made worse. No general reactions were seen. During the treatment the patient feels slight local irritation. Six hours later there is a feeling of fatigue at the site of the application. The reaction usually lasts 6 to 12 hours, and disappears completely in 24 hours. No skin manifestations were seen with the adopted dosage. After very long applications and with high intensity, however, vesicles similar to those seen in pemphigus may appear.

This paper indicates that high-frequency sound

vibration fills a gap in the physiotherapy of rheumatic diseases. Its main use is for resistant swellings, early ankylosis, periarthritis, and especially osteo-arthritis. It remains to be seen, however, whether the improvement will last, and what the permanent results will be.]

D. Gutmann.

Contribution to the Histopathology of Chronic Congestion of the Liver in Rheumatic Patients. (Contributo all'istopatologia del fegato da stasi cronica in soggetti rheumatici.) ANZI, M., and DONADELLI, F. (1947). *Arch. ital. Anat. Istol.*, **20**, 119.

The authors chose cases of rheumatic disease in which stasis of the liver and liver damage caused by the disease may both occur. They selected cases of acute rheumatic fever or circulatory failure of rheumatic origin, and compared them with cases where a rheumatic origin could be practically excluded. They investigated altogether 19 cases. The clinical facts were collected and anatomical and histological examinations carried out. Haematoxylin-eosin, Van Gieson, and Bielschowsky staining were used, with Weigert staining for fibrin if it was considered necessary.

It was found that in cases of rheumatic fever all components of the hepatic tissues were involved. Degenerative necrotic areas formed a map-like pattern independent of stasis. The necrotic parts had well-defined borders, within which a pattern of karyorrhexis could be observed. The haemorrhages were intense and the destruction of the parenchyma severe. The authors did not find the central fatty degeneration described by Heinrichsdorf, but they could not exclude the possibility that such degeneration had preceded the necrotic haemorrhagic stage. Diphtheria, acute endocarditis, pneumonia, streptococcal infections, peritonitis, arsphenamine, and toxaemia of pregnancy may produce the same histological picture. The authors believe that these changes are not the consequences of congestion, since they never observed in any of the non-rheumatic congestive cases this particular pattern of necrosis, and they believe that the lesions are caused by the specific rheumatic " noxa ".

E. Forrai.

Preliminary Note on the Use in Rheumatology of " Novocain " Combined with Polyvinylpyrrolidone in Concentrated Solution. (Note preliminaire sur l'emploi en rhumatologie de la novocaine associée a la polyvinylpyrolidone en solution concentrée.) DE SÈZE, S., ORDONNEAU, P., and DEUIL, R. (1947). *Rev. Rhum.*, **14**, 138.

In order to retard the rate of absorption of procaine (" novocain ") it has been combined with polyvinylpyrrolidone, and the authors have used 5-ml. ampoules containing a 2% solution of the former in a 20% solution of the latter. There was no reaction in a patient who previously had been intolerant of procaine.

T. G. Reah.

Rheumatic Manifestations Induced by Desoxycorticosterone Acetate Injections and Implants. (Manifestations rhumatismales provoquées par les injections ou les implants d'acétate de désoxycorticostérone.) DE GENNES, L., MAHOUDEAU, D., and BRICAIRE, H. (1947). *Bull. Soc. méd. Hôp. Paris*, **63**, 532.

Inflammation and swelling of various joints, accompanied by fever and increased erythrocyte sedimentation rate, were observed in 2 cases of Addison's disease. The picture was that of typical subacute rheumatic fever, which recurred when new or higher doses of desoxycorticosterone were given or implanted. In one of the patients the fever responded to intravenous salicylate but recurred afterwards. These observations are discussed in conjunction with experimental results of Selye, who produced inflammatory changes in the joints of rats with high doses of desoxycorticosterone. *H. Herxheimer.*

Influence of Sodium Salicylate on the Erythrocyte Sedimentation Rate. (Influence du salicylate de sodium sur la sédimentation des érythrocytes.) GALIMARD, J.-E. (1947). *Ann. Biol. clin.*, **5**, 239.

Samples of citrated blood from rheumatic patients were divided into four portions and enough sodium salicylate was added to each portion to give concentrations of 0, 0·02, 0·05, and 0·1% respectively. The erythrocyte sedimentation rate for each sample was determined by Homburger's method (*Amer. J. med. Sci.*, 1945, **210**, 168). The added salicylate tended to increase the sedimentation rate for blood from patients who were likely to benefit from salicylate therapy, and decrease it for those who were not. Nevertheless, if after addition of sodium salicylate the sedimentation rate invariably remains above normal and does not tend to fall, salicylate treatment is contraindicated.

It is suggested that the therapeutic action of salicylate in rheumatism is not due to antagonism of the sedimentation-rate-increasing activity of fibrinogen, since at the moment when the therapeutic activity of the salicylate was greatest an increase in the sedimentation rate was observed.

J. E. Page.

Skeletal Changes in Compressed Air Disease. (Skelettforandringar vid tryckulfsjuka.) SARTOR, E. (1947). *Nord. Med.*, **35**, 1551.

Aseptic necrosis of bones due to caisson disease is among the rarer non-malignant conditions affecting the skeletal system. The bones most frequently affected are long bones, such as the femur, tibia, and humerus, and 70% of the lesions are found in the lower limbs. Flat bones are not so frequently affected, possibly because of their relatively higher content of red marrow.

The pathogenesis is not fully understood, and it has not been possible to reproduce the condition experimentally, but it is considered that gas embolism or local liberation of nitrogen is followed by interference with nutrition, infarction proceeding to aseptic necrosis. The local reaction is one of resorption and recalcification, but incomplete resolution is shown by cystic areas bounded by a fibrous wall, which later becomes calcified. If near a joint the neighbouring cartilage becomes devitalized and arthritic changes develop.

The condition usually occurs in subjects over 40 years old who have worked under raised pressures for some years and who have on occasion been subjected to rapid decompression. Symptoms are usually referred to joints, and changes in the diaphysis of the bones are found on radiography. The picture is usually one of chronic osteo-arthritis of a joint with areas of necrosis and calcification in the adjoining bone. A typical case is described in a diver aged 40. Treatment is largely prophylactic. Early symptoms should be noted; recurrent symptoms mean that the individual affected should abandon that type of work. The fully developed condition may need orthopaedic treatment. The affection should be recognized from the medico-legal aspect and is of importance from the point of view of workman's compensation.

J. W. S. Lindahl.

Surgical Treatment of Rheumatism of the Knee. (Quelques points au sujet du traitement chirurgical du rhumatisme du genou.) ORY, — (1947). *Arch. Rhum.*, **7**, 76.

The author prefaces his article with notes on the anatomy, physiology, and pathology of the knee joint. The different aetiological factors are discussed. Operative treatment should be attempted only after exhaustion of all the available conservative methods. Three operative procedures are described: (a) Manipulation of the knee under general anaesthesia followed by a plaster dressing for three weeks, and bivalved later, with physiotherapy. A one-stage manipulation is preferable. Posterior capsulotomy or division of the hamstrings is sometimes added. (b) De-innervation of the knee, which the author has practised since 1943, mainly in cases with much pain. The technique of Tavernier is used by dividing the sensory branches at 1 or 2 mm. from the nerve. A diminution of the decalcification of bones was observed after this operation. (c) Femoropatellar arthroplasty. This operation was performed in 15 cases. Indications were (1) considerable formation of marginal exostoses of the patella, (2) the presence of articular loose bodies, and (3) tendency to ankylosis. The purpose of this operation is to diminish friction between the diseased cartilagenous surfaces. The joint is freely exposed from an incision 20 cm. above the knee joint. A pedicled fascial strip of the fascia lata is introduced into the joint from a lateral incision, interposed between the patella and the femoral condyles, and stitched in position. Immobilization for 6 or 7 days is followed by active physiotherapy. In all but one of his cases a range of movements of 110 to 130 degrees was restored, and all the patients had no difficulty in climbing stairs. *J. Koszyk.*

Low Back Pain. PAULETT, J. D. (1947). *Lancet*, **2**, 272.

The author describes the investigation at a military general hospital in Italy in 1944 of 25 cases of low back pain in which no organic disease was found. The patients all exhibited psychoneurosis or personality defect. No relationship was established between the pain and fibrositic nodules. It is suggested that these nodules are commonly found in normal muscle tissue. The artificial production of low back pain by injection of 0·2 ml. of 10% silver nitrate solution proved that these psychoneurotic subjects were not hypersensitive to painful stimuli, that their spontaneous backache was not due to painful muscle spasm, and that the backache was not perpetuated by conversion hysteria. The author comments on the similarity between this functional low backache and the inframammary pain of Da Costa's syndrome, and observes that both occur in the same type of patient. The mechanism of the backache is unknown.

Geoffrey McComas.

Public Health Aspects of Rheumatic Fever. KAISER, A. D. (1947). *N. Y. St. J. Med.*, **47**, 259.

The importance of rheumatic fever is shown by the fact that between the ages of 10 and 14 it is the leading cause of death, and from 15 to 25 is second only to tuberculosis. The incidence varies from country to country; thus, in Scandinavia (where it is notifiable) it is about 1 to 3 per thousand, in London about 1·8. In the U.S.A. there are more cases (3·5 to 7 per 1,000).

In the discussion Dr. J. G. Fred Hiss (Syracuse, N.Y.) puts forward the view that there is no difference in the incidence of rheumatic fever as between urban and rural areas; though, with the coming of the automobile, the hard-surfaced roads, and the central schools, there are few rural districts left in his State. He also emphasizes the importance of familiarizing both the layman and doctor with the earliest symptoms, particularly in children. *T. E. C. Early.*

Rheumatic Pneumonia. Report of Two Cases. MOSSBERGER, J. I. (1947). *J. Pediat.*, **30**, 113.

Rheumatic Pneumonia. SELDIN, D. W., KAPLAN, H. S., and BUNTING, H. (1947). *Ann. intern. Med.*, **26**, 496.

Scarlatinal Rheumatism. BERNARD, R., and RAYBAUD, P. (1947). *Pediatrie*, **36**, 407.

Common Forms of Arthritis and Rheumatism. HEALD, C. B. (1947). *N. Z. med. J.*, **46**, 497.

Relations of Nerve Roots to Abnormalities of Lumbar and Cervical Portions of the Spine. KEEGAN, J. J. (1947). *Arch. Surg., Chicago*, **55**, 246.

Urologic and Ophthalmologic Observations in Two Cases of Reiter's Syndrome. OLENICK, E. J., and SARGENT, J. W. (1947). *Nav. med. Bull., Wash.*, **47**, 657.

Osteoporosis Associated with Low Serum Phosphorus and Renal Glycosuria. COOKE, W. T., BARCLAY, J. A., GOVAN, A. D. T., and NAGLEY, L. (1947). *Arch. intern. Med.*, **80**, 147.

Reiter's Syndrome. A Report of Two Cases with Response in one to Large Doses of Mapharsen. KHOURY, E. N. (1947). *J. Urol.*, **58**, 268.

Polyarthritis and Senile Arteritis. (Polyarthrite et arterites seniles.) PAUZAT, D. (1947). *Rev. Rhum.*, **14**, 309.

The Present State of Treatment of Infantile and Juvenile Polyarthritis (Still's Disease and Deforming and Ankylosing Chronic Polyarthritis). (Etat actuel du traitement des polyarthrites infantiles et juveniles (Maladie de Still et polyarthrite chronique deformante et ankylosante).) GAROT, L. (1947). *Acta physiother. rheum. belg.*, **2**, 116.

Rheumatism and Diffuse Glomerular Nephritis. (Enfermedad reumatica y glomerulo-nefritis difusa.) VAISMAN, S., RAPAPORT, S., SCHÜLER P., TAPIA, A., and PENDOLA, L. (1947). *Rev. med. Chile.*, **75**, 177.

Hypertrophic Pulmonary Osteoarthropathy (Pierre Marie) and its Appearance as One of the Initial Symptoms of a Developing Pulmonary Neoplasm. (Sulla osteoartroadia ipertrofizzante pneumica di Pierre Marie e sul suo aparire fra i sintomi iniziali dello sviluppo di una neoplasia polmonare.) GALLI, T., and VITALE, E. (1947). *Ann. Radiol. diagnost.*, **19**, 3.

The Importance of Relapses in Rheumatism. (Importancia de las recidivas en la enfermedad reumática.) BAEZA GOÑI, A., SEPULVEDA DE BORQUEZ, H., and BARILARI, E. (1947). *Arch. Pediat. Uruguay.*, **18**, 57.

Thermal Treatment of Chronic Rheumatism. (Tratamento termal do reumatismo cronico.) MOURAO, M. DE FREITAS (1947). *Med. Cirurg. Farm.*, **136**, 454.

Treatment of Chronic Hydrarthrosis of the Knee-joint by Puncture and Irrigation with Ether. (Le traitement des hydarthroses chroniques du genou par la ponction et le brassage a l'ether sulfurique.) ROCHER, H. L. (1947). *Rev. Rhum.*, **14**, 302.

Arthrosis of the Shoulder. (Arthrose de l'epaule.) RIMBAUD, L., SERRE, H., PASSOUANT, P., and BOYER, F. (1947). *Rev. Rhum.*, **14**, 299.

" Suspension Therapy " Applied to Rheumatic Diseases. (La " Suspension Therapy " appliquee aux affections rhumatismales.) MICHOTTE, L. (1947). *Acta physiother. rheum. belg.*, **2**, 137.

Ultra-sound Therapy of Rheumatic Diseases. (Ultraschalltherapie rheumatischer Erkrankungen.) HINTZELMANN, U. (1947). *Dtsch. med. Wschr.*, **72**, 350.

Biological Fever Therapy in Inflammatory Rheumatism. (Piretoterapía biólogica en reumatismos inflamatorios.) FRANCE, O., and LOSDA, M. (1947). *Rev. argent. Reum.*, **12**, 72.

Preliminary Report on a Psychosomatic Study of Rheumatoid Arthritis. JOHNSON, A., and ALEXANDER, F. (1947). *Psycosom. Med.*, **9**, 295.

Psychogenic Rheumatism. WEISS, E. (1947). *Ann. intern. Med.*, **26**, 890.

Tuberculous Rheumatism. GRABER-DUVERNAY, J. (1947). *Rev. Rhum.*, **14**, 335.

Osteo-articular Brucellosis. RIMBAUD, L., and SERRE, H. (1947). *Rev. Rhum.*, **14**, 321.

Prophylaxis of Cardiac Irradiation in Rheumatic Children in Uruguay. DELGADO CORREA, B., and MACCIO, O. (1947). *Rev. argent. Reum.*, **12**, 190.

Treatment of Degenerative Types of Rheumatism. M. LOSADA. (1947). *Rev. argent. Reum.*, **12**, 186.

Hip Joint Reconstruction by Vitallium Mould Arthroplasty. LAW, W. A. (1948). *Rheumatism*, **3**, 157.

The Measurement of Bone Opacity. BYWATERS, E. G. L. (1948). *Clin. Sci.*, **6**, 281.

Clinico-social Study of Rheumatism Based on 425 Observations. (Estudio clinico-social del reumatismo y aportacion de 425 observaciones.) FERNANDES, M. M. F., TORRES RUIZ, A., and GUTIERREZ DEL OLMO, J. *Med. colon.*, **11**, 20.

Rheumatism in the Writings of Celsus. (Las afecciones reumáticas en la obra de Celso.) MORENO, A. R. (1947). *Bol. Liga argent. Reum.*, **10**, 43.

The Pathology of Rheumatic Diseases. ANGEVINE, D. M. (1947). *Radiology*, **49**, 1.

Chronic Rheumatic Diseases. WHELTON, A. (1947). *J. med. Ass., Eire*, **21**, 7.

Rheumatic Diseases: A Challenge and an Opportunity. COHEN, H. (1947). *Proc. roy. Soc. Med.*, **40**, 443. [This article should be read in full in the original.]

BOOK REVIEWS

Die Sauna. Geschichte-Grundlagen ihrer Wirkung. An wendung sur Prophylaxe und Therapie. Mit Anhang über Bau und Betrieb der Sauna. By V. R. Ott. 1948. Benno Schwabe and Co. Basle. Pp. 224: 29 illustrations. Price 15 fr.

The Finnish Sauna is a form of bath with supposed panacean properties in which hot air, steam, hot water, flagellation, hot and cold douche, etc., play a role. It seems primitive in design, consisting of a room in which is a stone oven and tiers of benches for patients. There is a chimney for coal fuel, none for wood. Electrical heat may be used. The vapour charge of the air varies and the temperature may reach 80° C. or more. Bursts of steam are let off now and then from water poured on the hot stones. The process dates, with variations, from the Roman bath. Finland seems to have been the chief country of maintenance and of evolution into the present form. There it has been used for many ills, and systematically for restoration of energy after laborious work. Switzerland and Germany now make much use of it.

Dr. Ott introduced this sweat bath into the thermal station at Zürich in 1941. He now gives a faithful account of his experience with it and details of its action on the various organs and systems. The nervous (autonomic), circulatory, and renal systems are markedly stimulated by the bath and react favourably in the many forms of rheumatism, in affections of bone, muscle, and joints, in catarrh, and in various infections. Contra-indications are few, and include uncompensated heart affections, severe hypertension, pulmonary tuberculosis, and severe nephritis. The great improvement observed in the defences and resistance of the organism as a result of its use are mediated by changes of tone produced in the autonomic system. Immunity from the ill effects of climatic change is also set up by it.

The immediate changes produced in the blood and circulation are distinctive; blood sugar and sedimentation rate are increased, alkali reserve is diminished in most cases. The blood picture shows significant changes. Heart rate and blood pressure are raised, and also the body temperature. Installation methods are described.

D. T. BARRY.

Diseases of the Joints and Rheumatism. By Kenneth Stone. 1947. William Heinemann. London. Pp. 362. Illustrated, with 16 coloured plates. Price 30*s.* net.

Until recent years there has been a dearth of textbooks on the subject of rheumatism, and this one differs from the others in treating the subject from the physiological and pathological angles. It is more suited to the post-graduate, reading for higher qualifications, or for the specialist as a book of reference, than for the student.

The first chapter, on " classification", is in the nature of an essay on classification in general, and at the same time it epitomizes the various views of rheumatism from Hippocrates down to the present day. Perhaps it would have been better if this chapter had been at the end of the book, for the author does not state clearly which classification he recommends, and also, during the rest of the book, he does not adhere to the classification he details.

The chapters on the general anatomy and physiology of joints, and how to examine joints, are excellent, and the one on chronic strain of ligaments contains a valuable chart illustrating defective posture in children. He is on firm ground when he describes the pathology of the various lesions, and his dismissal of the allergic reaction in favour of a virus infection as the causative agent in rheumatoid arthritis is worthy of respect.

The historical references are very interesting and show that the author has made an exhaustive study of classical and continental—particularly French—literature.

The chapter on diseases of the spine is comprehensive, and the frequency with which tuberculosis of the spine is mistaken for arthritis of rheumatic origin is rightly stressed. The description of how to examine the spine is useful, but the diagram, showing different normal movements, is difficult to follow.

Throughout the book, the treatments described follow conventional lines, but there are notable omissions of useful therapeutic measures, such as blood transfusion and insulin in rheumatoid arthritis, or bismuth injections as an alternative to gold therapy. No doubt Dr. Stone was wise to omit all mention of intra-articular injections in osteo-arthritis, as the value of this treatment is still *sub judice*. (Incidentally, the diagram showing aspiration of a knee joint seems to be somewhat elementary to include in a book of this calibre.)

The second part of the book is devoted entirely to muscular rheumatism and fibrositis, and the theory is advanced that rheumatic myalgia is the result of vagatonia, which is influenced by infective, toxic, endocrine, and emotional agents. Reasoned arguments and details of experiments substantiate this theory. More research on these lines might be profitable.

The chapter on fibrositis is incomplete, for there is no reference to the work of Copeman and Ackerman, or to that of Gibson, Kersley, and Desmarais ; but there is an adequate précis of the work of Lewis and Kellgren on somatic pain.

In the last few pages the author courageously enters the sciatica controversy, and links the name of Cotugno with this symptom complex, finally allying Cotugno's " nervous sciatica " with the disc syndrome.

The book is well printed on excellent paper, and copiously illustrated, and the reproductions—particularly of the photomicrographs—are beyond criticism.

W. YEOMAN.

EMPIRE RHEUMATISM COUNCIL

ELEVENTH ANNUAL REPORT

The Eleventh Annual Report of the Empire Rheumatism Council, covering the period from November, 1946, to October, 1947, was recently presented by the Right Hon. Lord Horder, who said:

"It is with sincere pleasure that I once again extend a cordial welcome to the Members of the Empire Rheumatism Council at the Annual General Meeting—the eleventh since the Council's inception. My first duty must be to report with gratification the receipt from our Royal President, H.R.H. The Duke of Gloucester, of a message of encouragement to us in the arduous tasks upon which we are engaged, and conveying His Royal Highness's best wishes for the success of our further activities and his hope of meeting us again personally in the new year.

Research

The investigation into the factors of the causation of rheumatoid arthritis, referred to in my Report last year, is being maintained; it is as yet too early to draw conclusions from this research. A new directive is being carefully prepared by our Scientific Committee which it is hoped will reveal valuable information to the Statistician in framing his final analytical report. The Council has at present fourteen 'registrars' at work on this research.

I am glad to be able to record the re-opening of the Council's Laboratory at the Hospital of St. John and St. Elizabeth, and the appointment by the Council of a research worker to study the allergic aspects of rheumatism under the direction of Profs. Rimington and Cameron. It will be recalled that the Council expended a considerable sum of money upon this laboratory in 1938, but the unforeseen outbreak of hostilities in 1939 caused a cessation of our work there.

Treatment

The contributions to the rheumatism department of the West London Hospital have continued owing to the co-operation of the Boroughs of Kensington, Hammersmith, and Fulham at the same level as in 1946, whilst payments from the Scottish Fund to Prof. Davidson for his department in Edinburgh have been renewed.

Consultation with the Ministry of Health on the Council's suggested scheme for the Regional organization of treatment facilities under the forthcoming National Health Act have been amicably maintained.

Many new methods of treatment have been submitted to the Council. These have all been submitted to the Research and Investigation Sub-Committee and reported upon. Nothing of value has emerged during this year. In view of the increasing national interest in the treatment of the chronic sick, Lord Amulree (Ministry of Health) has joined this Sub-Committee.

Education

In the field of education we have also been active. In June last a postgraduate course was held at the Apothecaries Hall, on June 13, 14, and 15 and was well attended. A further postgraduate course arranged for November last was also highly successful; over a hundred medical men attended. It is considered by the Council to be most important that the postgraduate courses should become a leading feature of our educational facilities, providing as they do a stimulus to the formation of the nucleus of a body of medical men trained in the rheumatic diseases.

During the year the Nuffield Foundation decided to offer Fellowships in chronic rheumatism, and the Council's offer of collaboration at any time was cordially received by the Trustees.

The Fifth Edition of 'Rheumatism—A Plan for National Action' was issued during the year, and copies have been presented to the Chairmen of the Regional Boards appointed under the National Health Service and, as is customary, to the medical libraries. Copies are available on application (price 2*s*. 6*d*.). Films and leaflets have also been a feature of the year's educational activities.

Relations at Home

The Navy.—As testimony to the value placed upon the views of the Empire Rheumatism Council in matters of rheumatology, it must be put on record that the Director-General of the Medical Department of the Navy has expressed a desire that the Council should tender advice and assistance if at any time problems relating to rheumatism again arise in that Service. We were only too ready to acquiesce and have conveyed the assurance that the Council would be prepared at all times to afford the benefit of its assistance in the form of scientific advice, etc.

The Medical Research Council have re-appointed their three representatives on our Scientific Advisory Committee. Their co-operation in this matter is much valued by our Council.

The National Coal Board.—The Honorary Medical Secretary was invited to a conference called in Newcastle by Lord Citrine. At a subsequent meeting of the Rheumatism Committee, formed by the National Coal

Board and Miner's Welfare Commission, to which the Honorary Medical Secretary was appointed, it was agreed to recommend that the pilot survey into the incidence and causes of rheumatism amongst miners, suggested by the Empire Rheumatism Council, be carried out in certain coalfield areas. The new rheumatism research department of the University of Manchester (Nuffield Foundation) agreed to carry this out with their newly appointed Director (Dr. Kellgren). Dr. Kellgren has also joined the Council's Scientific Advisory Committee as official representative of this important new department.

Ministry of Food.—A recommendation of our Scientific Advisory Committee that extra milk should be made available for cases of active rheumatoid arthritis has been agreed by the Ministry of Food Advisory Committee. The Ministry have adopted our proposal that this group of sufferers shall be defined for the purpose as 'polyarthritis associated with anaemia, loss of weight, and an erythrocyte sedimentation rate of more than 15 mm. (Westergren)'.

Ministry of Labour.—As a result of an approach by the Empire Rheumatism Council to the Ministry of Labour and National Service, chronic arthritic patients have been accepted as eligible for admission to the new rehabilitation centres and 'remploy' factories which are established at Papworth and Enham under the Disabled Persons Employment Act, on the same terms as those applicable to chronic tuberculous and chronic cardiac diseases, and other remploy factories not restricted to these diseases.

Provinces.—Coming now to provincial liaison matters, the Empire Rheumatism Council was invited by the Leamington Spa Medical Advisory Committee and the County Council to put forward plans whereby a practical contribution could be made under the National Health Service Act to the campaign against rheumatism. On the advice which the Empire Rheumatism Council was able to submit the authorities concerned have expressed their appreciation of what they consider will prove of great value in formulating a long-term plan for the development of the special facilities they desire.

The Honorary Medical Secretary has visited Leeds at the invitation of the University Committee which is planning a Regional scheme of research and treatment under Professor Hartfall, and made a report. He was also invited as representative of the Scientific Advisory Committee to attend a meeting at the Devonshire Royal Hospital, Buxton, regarding their liaison with the Manchester scheme.

Relations Abroad

Canada.—The past year has been one of much activity and progress in the matter of developing relations with our Empire.

It was our privilege to welcome in August last, Dr. W. S. Barnhart, M.D., Secretary to the Canadian Rheumatism Association. We were able to extend facilities and introductions to enable him to see as much as possible, in the short time at his disposal, of what was being done in this country in the matter of research into and treatment of, the rheumatic diseases. Recent intimations from Dr. Barnhart inform us of the successful outcome of the National Conference on Rheumatic Diseases, convened by the Canadian Government in response to a public request, which was held in Ottawa in October last; also of the establishment of a Canadian Arthritis and Rheumatism Society and that the charter and by-laws governing their activities will be formulated along the lines of the advice tendered by the Empire Rheumatism Council. The Canadian Society hope it may be possible for a representative of the Empire Rheumatism Council to be present at their inaugural Meeting early next year. This means that Canada is continuing to follow the lead of the Empire Rheumatism Council.

New Zealand and Australia.—We have been encouraged to learn from Dr. C. B. Heald of his progress in New Zealand in endeavouring to arrange for the Medical Authorities in that Dominion to form an official Rheumatism Council in association with the Empire Rheumatism Council; and steps to inaugurate a similar Council in Australia are also in hand. Subsequent to Dr. Heald's visit we have at his request sent literature to the Department of Health, Wellington, New Zealand.

Expressions of appreciation have been received from the University of Otago, Dunedin, New Zealand, for the help we continue to render their Medical School Library.

European League.—In countries not within the orbit of the British Empire there has also been much activity during the past year.

The European League against Rheumatism held its first Congress in Copenhagen from Sept. 3 to 7. Twenty-five countries were represented by nearly four hundred delegates. The official delegates from the British Section were our Honorary Medical Secretary and Dr. G. D. Kersley, a member of our Scientific Advisory Committee. The Council of the League are actively interested in making our Journal, *The Annals of the Rheumatic Diseases*, the vehicle for their activities instead of restarting the *Acta Rheumatalogica*. A British Branch of the League has been formed under our auspices to co-operate with the International and the European branch.

America.—A request was received from Dr. Ralph Pemberton, of Philadelphia, for aid in connexion with the International Congress on Rheumatic Diseases to be held in America in the Spring of 1949.* We were able to furnish Dr. Pemberton with several papers and suggestions on general scientific matters, and these have been gratefully acknowledged by him as a valuable initial contribution to his programme. Dr. Robert Stecher, the President of the American Rheumatism Association, recently paid a visit to this country. The Council were able to be of some assistance to him, and he has subsequently expressed his gratitude for this help. Several other members of the association, including Dr. Otto Steinbrocker, have also been welcomed by the Council.

It is of interest also to record that the Helen Hay Witney Foundation, recently established in New York to further basic research in the field of rheumatic fever, has applied to our Council for literature regarding our activities to assist them in their future work.

The American Branch of the International League

* This, the most important Congress of the kind ever held, will take place in New York, in June, 1949.—EDITOR.

against Rheumatism are also proposing to adopt *The Annals of the Rheumatic Diseases* as their medium of publication in association with the Empire Rheumatism Council.* The Council look upon this as a valuable form of collaboration between these two countries on the scientific level.

It will therefore be seen that the evidence of a revival of interest in the problems of rheumatism abroad referred to in my last Annual Report is being translated in a very real and practical manner, and that our Council is playing its part.

Standard Case Sheet

During the year a standard case sheet for the rheumatic diseases has been drawn up and approved after much careful deliberation, and it is hoped that this will shortly be in use in many centres throughout the Kingdom.

Administration

It is recommended that the key administrative Committees, viz: Executive Committee, the Scientific Advisory Committee, and the Finance Committee—should be re-elected for 1948. I am sure I am voicing the opinion of the Council in expressing satisfaction with the present financial position in relation to last year.

The Future

The past year was characterized by difficulties of a novel quality which it is hoped will not be manifest during 1948. Given a year free from unusual handicaps I look forward with confidence, not only to a continued expansion of our activities both at home and in the Empire, but to a development to a degree not touched for several years. Since the momentum of our work is dependent solely upon our income, we hope that we may receive financial assistance in an even greater measure during 1948 as the most vital contribution to the solving of the rheumatic problem—a problem which affects over two million of our fellow citizens in the British Isles alone. Without the financial support of our many friends and sympathizers, nothing can be done; with their continued help and the recruitment of new contributors there is good cause to believe that the problem of rheumatic disease can be largely solved by persevering effort.

It may be pointed out here that, although the National Health Act will presumably come into force next year, this will not affect the need of this Council for funds with which to prosecute research, since the provisions of the Act only cover the question of treatment and not (at any rate at present) of research.

The achievements of the past year have been due to the team spirit and diligent devotion of each member of the various Committees operating within our Constitution.

Whilst it would be invidious of me to single out for mention any special name, I cannot close this report without testifying to the fact that the Council are indeed fortunate to number amongst its counsellors Sir Walter Kinnear, Chairman of the Finance Committee, Professor L. S. P. Davidson, Chairman of the Scientific Advisory Committee, Dr. W. S. C. Copeman, Honorary Medical Secretary, Dr. B. Schlesinger, Chairman of the Research and Investigation Sub-Committee and Dr. F. D. Howitt, Chairman of the Education and Development Sub-Committee. The Council appreciates highly the great help it has received from its General Secretary, Mr. Victor Howell, and from his very limited staff."

* The *Annals of the Rheumatic Diseases* will also be used as the medium of expression of the Canadian Medical Association.—EDITOR.

OBITUARY

We regret to record that Professor Pierre-Marie Besse, honorary professor at the University in Geneva, and former professor in physiotherapy and medical hydro-climatology, died on May 3, 1948. This sad news comes from Professor Walthard from the Institut de Physiatrie at the University of Geneva. Professor Besse was a highly regarded physiotherapist in Switzerland, and was very interested in European co-operation within the field of rheumatology.